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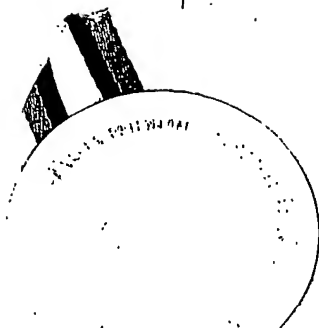
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Method and kits for investigating cancer

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06. Okt. 2003**METHODS AND KITS FOR INVESTIGATING CANCER****TECHNICAL FIELD OF THE INVENTION**

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The present invention relates to methods and compositions for the prediction of therapy outcome (e.g. tumor response to therapy), diagnosis, prognosis, prevention and treatment of neoplastic diseases. Cancer cells display a specific pattern of gene expression related to their morphological type, state of progression, acquirement of genomic alterations, point mutations in critical genes such as gatekeepers and tumor suppressors or due to the dependency of external signals such as growth factors, hormones or other secondary messengers.

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The invention discloses genes which show an altered expression in a particular neoplastic tissue compared to the corresponding healthy tissue or to other neoplastic lesions unresponsive to a given chemotherapy. They are useful as diagnostic markers and could be also regarded as therapeutically targets. Methods are disclosed for predicting, diagnosing and prognosing as well as preventing and treating neoplastic disease. The genes disclosed in this invention have been identified in breast cancers but are predictable of outcome to a certain therapy regimen and therefor they are also relevant for other types of cancers in tissues other than breast.

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**BACKGROUND OF THE INVENTION AND PRIOR ART**

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Cancer is the second leading cause of death in the United States after cardiovascular disease. One in three Americans will develop cancer in his or her lifetime, and one of every four Americans will die of cancer. More specifically breast cancer claims the lives of approximately 40,000 women and is diagnosed in approximately 200,000 women annually in the United States alone. Cancer are classified based on different parameters, such as tumor size, invasion status, involvement of lymph nodes, metastasis, histopathology, immunohistochemical markers, and molecular markers

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(WHO. International Classification of diseases (1); Sabin and Wittekind, 1997 (2)). With the recent advances in gene chip technology, researchers are increasingly focusing on the categorization of tumors based on the distinct expression of marker genes Sorlie et al., 2001 (3); van 't Veer et al., 2002 (4).

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Chemotherapy remains a mainstay in therapeutic regimens offered to patients with breast cancer, particularly those who have cancer that has metastasized from its site of origin (Perez, 1999, (5)). There are several chemo-therapeutic agents that have demonstrated activity in the treatment of breast cancer and research is continuously  
10 in an attempt to determine optimal drugs and regimens. However, different patients tend to respond differently to the same therapeutic regimen. Currently, the individuals response to certain therapy can only be assessed statistically, based on data of former clinical studies. There are still a great number of patients who will not benefit from a systemic chemotherapy. Especially, breast cancers are very  
15 heterogeneous in their aggressiveness and treatment response. They contain different genetic mutations and variations affecting growths characteristic and sensitivity to several drugs. Identification of each tumor's molecular fingerprint, then, could help to segregate patients who have particularly aggressive tumors or who need to be treated with specific beneficial therapies. As research involving genetics and associated  
20 responses to treatment matures, standard practice will undoubtedly become more individualized, enabling physicians to provide specific treatment regimens matched with a tumor's genetic profiles to ensure optimal outcomes.

### **SUMMARY OF THE INVENTION**

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The present invention relates to the identification of 165 human genes being differentially expressed in neoplastic tissue resulting in an altered clinical behavior of a neoplastic lesion. The differential expression of these 165 genes is not limited to a specific neoplastic lesion in a certain tissue of the human body.

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In preferred embodiments of this invention the neoplastic lesion, of which these 165 genes are altered in their expression is a cancer of the human breast. This cancer is not limited to females and may also be diagnosed and analyzed in males.

5 The invention relates to various methods, reagents and kits for diagnosing, staging, prognosis, monitoring and therapy of breast cancer. "Breast cancer" as used herein includes carcinomas, (e.g., carcinoma in situ, invasive carcinoma, metastatic carcinoma) and pre-malignant conditions, neomorphic changes independent of their histological origin (e.g. ductal, lobular, medullary, mixed origin). The compositions, methods, and kits of the present invention comprise comparing the level of mRNA  
10 expression of a single or plurality (e.g. 2, 5, 10, or 50 or more) of genes (hereinafter "marker genes", listed in Table 1, SEQ ID NO:1 to 165, the respective polypeptide sequences coded by them are numerated SEQ ID NO:166 to 330, see also Table 1) in a patient sample, and the average level of expression of the marker gene(s) in a  
15 sample from a control subject (e.g., a human subject without breast cancer). A preferred sub-set of marker genes representing a specific test composition or kit is listed in Table 2.

20 The invention relates further to various compositions, methods, reagents and kits, for prediction of clinically measurable tumor therapy response to a given breast cancer therapy. The compositions, methods, and kits of the present invention comprise comparing the level of mRNA expression of a single or plurality (e.g. 2, 5, 10, or 50 or more) of breast cancer marker genes in an unclassified patient sample, and the average level of expression of the marker gene(s) in a sample cohort comprising  
25 patient responding in different intensity to an administered breast cancer therapy. In preferred embodiments of this invention the specific expression of the marker genes can be utilized for discrimination of responders and non-responders to an anthracycline based (e.g. polychemotherapies with epirubicin or doxorubicin) chemo-therapeutic intervention.

In further preferred embodiments, the control level of mRNA expression is the average level of expression of the marker gene(s) in samples from several (e.g., 2, 3, 4, 5, 8, 10, 12, 15, 20, 30 or 50) control subjects. These control subjects may either be not affected by breast cancer or be identified and classified by their clinical response prior to the determination of their individual expression profile.

As elaborated below, a significant change in the level of expression of one or more of the marker genes (set of marker genes) in the patient sample relative to the control level provides significant information regarding the patient's breast cancer status and responsiveness to chemotherapy. In the compositions, methods, and kits of the present invention the marker genes listed in Table 1 may also be used in combination with well known breast cancer marker genes (e.g. CEA, mammaglobin, or CA 15-3).

According to the invention, the marker gene(s) and marker gene sets are selected such that the positive predictive value of the compositions, methods, and kits of the invention is at least about 10%, preferably about 25%, more preferably about 50% and most preferably about 90%. Also preferred for use in the compositions, methods, and kits of the invention are marker gene(s) and sets that are differentially expressed, as compared to normal breast cells, by at least the minimal mean differential expression factor presented in Table 3, in at least about 20%, more preferably about 50% and most preferably about 75% of any of the following conditions: stage 0 breast cancer patients, stage I breast cancer patients, stage II breast cancer patients, stage III breast cancer patients, stage IV breast cancer patients, grade I breast cancer patients, grade II breast cancer patients, grade III breast cancer patients, malignant breast cancer patients, patients with primary carcinomas of the breast, and all other types of cancers, malignancies and transformations associated with the breast.

The detection of marker gene expression is not limited to the detection within a primary, secondary or metastatic lesion of breast cancer patients, and may also be detected in lymphnodes affected by breast cancer cells or minimal residual disease

cells either locally deposited (e.g. bone marrow, liver, kidney) or freely floating throughout the patients body.

5 In one embodiment of the compositions, methods, reagents and kits of the present invention, the sample to be analyzed is tissue material from neoplastic lesion taken by aspiration or punctuation, excision or by any other surgical method leading to biopsy or resected cellular material. In one embodiment of the compositions, methods, and kits of the present invention, the sample comprises cells obtained from the patient. The cells may be found in a breast cell "smear" collected, for example, by  
10 a nipple aspiration, ductal lavage, fine needle biopsy or from provoked or spontaneous nipple discharge. In another embodiment, the sample is a body fluid. Such fluids include, for example, blood fluids, lymph, ascitic fluids, gynecological fluids, or urine but not limited to these fluids.

15 In accordance with the compositions, methods, and kits of the present invention the determination of gene expression is not limited to any specific method or to the detection of mRNA. The presence and/or level of expression of the marker gene in a sample can be assessed, for example, by measuring and/or quantifying of:

- 20 1) a protein encoded by the marker gene in Table 1 (SEQ ID NO:1 to 165) or a polypeptide comprising a polypeptide selected from SEQ ID NO:166 to 330 or a polypeptide resulting from processing or degradation of the protein (e.g. using a reagent, such as an antibody, an antibody derivative, or an antibody fragment, which binds specifically with the protein or polypeptide),
- 25 2) a metabolite which is produced directly (i.e., catalyzed) or indirectly by a protein encoded by the marker gene in Table 1 (SEQ ID NO:1 to 165) or by a polypeptide comprising a polypeptide selected from SEQ ID NO:166 to 330,
- 30 3) a RNA transcript (e.g., mRNA, hnRNA) encoded by the marker gene in Table 1, or a fragment of the RNA transcript (e.g. by contacting a mixture of RNA

transcripts obtained from the sample or cDNA prepared from the transcripts with a substrate having nucleic acid comprising a sequence of one or more of the marker genes listed within Table 1 fixed thereto at selected positions). The mRNA expression of these genes can be detected e.g. with DNA-microarrays as provided by Affymetrix Inc. or other manufacturers. U.S. Pat. No. 5,556,752. In a further embodiment the expression of these genes can be detected with bead based direct fluorescent readout techniques such as provided by Luminex Inc. PCT No. WO 97/14028.

10 In one aspect, the present invention provides a composition, method, and kit of assessing whether a patient is afflicted with breast cancer (e.g., new detection or "screening", detection of recurrence, reflex testing, especially in patients having an enhanced risk of developing breast cancer (e.g., patients having a familial history of breast cancer and patients identified as having a mutant onco-gene). For this purpose  
15 the composition, method, and kit comprises comparing:

- a) the level of expression of a single or plurality of marker genes in a patient sample, wherein at least one (e.g. 2, 5, 10, or 50 or more) of the marker genes is selected from the marker genes of Table 1 and
- 20 b) the normal level of expression of the marker gene in a control subject without breast cancer.

A significant increase as well as decrease in the level of expression of the selected  
25 marker genes (e.g. 2, 5, 10, or 50 or more) in the patient sample relative to each marker gene's normal level of expression is an indication that the patient is afflicted with breast cancer.

The composition, method, and kit of the present invention is also useful for  
30 prognosing the progression or the outcome of the malignant neoplasia. For this purpose the composition, method, and kit comprises comparing

- a) the level of expression of a single or plurality of marker genes in a patient sample, wherein at least one (e.g. 2, 5, 10, or 50 or more) of the marker genes is selected from the marker genes of Table 1

5

- b) a control pattern of expression of these marker genes.

The composition, method, and kit of the present invention is particularly useful for identifying patients who will respond to a certain chemotherapy. For this purpose the composition, method, and kit comprises comparing

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- a) the level of expression of a single or plurality of marker genes in a patient sample, wherein at least one (e.g. 2, 5, 10, or 50 or more) of the marker genes is selected from the marker genes of Table 1 and

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- b) the level of expression of the marker gene in a control subject. The control subject may either be not affected by breast cancer or be identified and classified by their clinical response to the particular chemotherapy.

20

In another aspect, the invention provides a composition, method, and kit of assessing the efficacy of a therapy for inhibiting breast cancer in a patient. This composition, method, and kit comprises comparing:

- a) expression of a single or plurality of marker genes in a first sample obtained from the patient prior to any treatment of the patient, wherein at least one of the marker genes is selected from the marker genes listed within Table 1 and

25

- b) expression of the marker gene in a second sample obtained from the patient following at least one dose of the therapy.

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It will be appreciated that in this composition, method, and kit the "therapy" may be any therapy for treating breast cancer including, but not limited to, chemotherapy, anti-hormonal therapy, directed antibody therapy, radiation therapy and surgical removal of tissue, e.g., a breast tumor. Thus, the compositions, methods, and kits of  
5 the invention may be used to evaluate a patient before, during and after therapy, for example, to evaluate the reduction in tumor burden.

In a further aspect, the present invention provides a composition, method, and kit for monitoring the progression of breast cancer in a patient. This composition, method,  
10 and kit comprising:

- a) detecting in a patient sample at a first time point, the expression of a single or plurality of marker genes, wherein at least one of the marker genes is selected from the marker genes listed in Table 1  
15
- b) repeating step a) at a subsequent time point in time; and
- c) comparing the level of expression of each marker gene detected in steps a) and b), and therefrom monitoring the progression of breast cancer in the  
20 patient.

In another aspect, the invention provides a composition, method, and kit for *in vitro* selection of a therapy regime (e.g. the kind of chemotherapeutical argents) for inhibiting breast cancer in a patient. This composition, method, and kit comprises the  
25 steps of:

- a) obtaining a sample comprising cancer cells from the patient;
- b) separately maintaining aliquots of the sample in the presence of a diverse test  
30 compositions;



- c) comparing expression of a single or plurality of marker genes, selected from the marker genes listed in Table 1;

in each of the aliquots; and

5

- d) selecting one of the test compositions which induces a lower level of expression of genes from SEQ ID 11, 17, 22, 25, 31, 36, 48, 49, 57, 83, 107, 108, 112, and 159 and/or a higher level of expression of genes from SEQ ID 24, 47, 54, 58, 59, 60, 67, 79, 80, 88, 114, 118, 135, and 141 in the aliquot containing that test composition, relative to the level of expression of each marker gene in the aliquots containing the other test compositions.

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The invention further provides a composition, method, and kit of assessing the carcinogenic potential of a certain biological or chemical compound. This composition, method, and kit comprises the steps of:

15

- a) maintaining separate aliquots of breast cells in the presence and absence of the test compound; and

20

- b) comparing expression of a single or plurality of marker genes in each of the aliquots, wherein at least one of the genes is selected from the marker genes listed within Table 1. A significant increase in the level of expression of genes from SEQ ID 19, 23, 36, 45, 62, 74, 81, 96, 103, 106, 107, 112, 113, and 132 and/or a significant decrease of genes from SEQ ID 22, 25, 31, 40, 43, 47, 55, 57, 59, 60, 108, 119, 121, 124, 154, 156, 157, 158, 159, 160, 162, and 164 in the aliquot maintained in the presence of (or exposed to) the test compound, relative to the level of expression of each marker gene in the aliquot maintained in the absence of the test compound, is an indication that the test compound possesses breast carcinogenic potential.

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The invention further provides a composition, method, and kit of treating a patient afflicted with breast cancer. This composition, method, and kit comprises providing to cells of the patient an antisense oligonucleotide complementary to a polynucleotide sequence of a marker gene listed within Table 1

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The invention additionally provides a composition, method, and kit of inhibiting breast cancer cells in a patient at risk for developing breast cancer. This composition, method, and kit comprises inhibiting expression of a marker gene listed in Table 1.

10 In yet another embodiment the invention provides compositions, methods, and kits of screening for agents which regulate the activity of a polypeptide comprising a polypeptide selected from SEQ ID NO: 166 to 330. A test compound is contacted with the particular polypeptide. Binding of the test compound to the polypeptide is detected. A test compound which binds to the polypeptide is thereby identified as a  
15 potential therapeutic agent for the treatment of malignant neoplasia and more particularly breast cancer.

In even another embodiment the invention provides another composition, method, and kit of screening for agents which regulate the activity of a polypeptide  
20 comprising a polypeptide selected from SEQ ID NO: 166 to 330. A test compound is contacted with the particular polypeptide . A biological activity mediated by the polypeptide is detected. A test compound which decreases the biological activity is thereby identified as a potential therapeutic agent for decreasing the activity of the particular polypeptide in malignant neoplasia and especially in breast cancer A test  
25 compound which increases the biological activity is thereby identified as a potential therapeutic agent for increasing the activity of the particular polypeptide in malignant neoplasia and especially in breast cancer

The invention thus provides polypeptides selected from one of the polypeptides with  
30 SEQ ID NO: 166 to 330 which can be used to identify compounds which may act, for example, as regulators or modulators such as agonists and antagonists, partial

agonists, inverse agonists, activators, co-activators and inhibitors of the polypeptide comprising a polypeptide selected from SEQ ID NO: 166 to 330. Accordingly, the invention provides reagents and compositions, methods, and kits for regulating a polypeptide comprising a polypeptide selected from SEQ ID NO: 166 to 330 in malignant neoplasia and more particularly breast cancer. The regulation can be an up- or down regulation. Reagents that modulate the expression, stability or amount of a polynucleotide listed in Table 1 (SEQ ID NO: 1 to 165) or the activity of the polypeptide comprising a polypeptide selected from SEQ ID NO: 166 to 330 can be a protein, a peptide, a peptidomimetic, a nucleic acid, a nucleic acid analogue (e.g. peptide nucleic acid, locked nucleic acid) or a small molecule. Compositions, methods, and kits that modulate the expression, stability or amount of a polynucleotide comprising a polynucleotide selected from SEQ ID NO: 1 to 165 (listed in Table 1) or the activity of the polypeptide comprising a polypeptide selected from SEQ ID NO: 166 to 330 (Table 1) can be gene replacement therapies, antisense, ribozyme and triplex nucleic acid approaches.

The invention further provides a composition, method, and kit of making an isolated hybridoma which produces an antibody useful for assessing whether a patient is afflicted with breast cancer. The composition, method, and kit comprises isolating a protein encoded by a marker gene listed within Table 1 or a polypeptide fragment of the protein, immunizing a mammal using the isolated protein or polypeptide fragment, isolating splenocytes from the immunized mammal, fusing the isolated splenocytes with an immortalized cell line to form hybridomas, and screening individual hybridomas for production of an antibody which specifically binds with the protein or polypeptide fragment to isolate the hybridoma. The invention also includes an antibody produced by this method. Such antibodies specifically bind to a full-length or partial polypeptide comprising a polypeptide selected from SEQ ID NO: 166 to 330 (listed in Table 1) for use in prediction, prevention, diagnosis, prognosis and treatment of malignant neoplasia and breast cancer in particular.

Yet another embodiment of the invention is the use of a reagent which specifically binds to a polynucleotide comprising a polynucleotide selected from SEQ ID NO: 1 to 165 or to a polypeptide comprising a polypeptide selected from SEQ ID NO: 166 to 330 (listed in Table 1) in the preparation of a medicament for the treatment of malignant neoplasia and breast cancer in particular.

Still another embodiment is the use of a reagent that modulates the activity or stability of a polypeptide comprising a polypeptide selected from SEQ ID NO: 166 to 330 (Table 1) or the expression, amount or stability of a polynucleotide comprising a polynucleotide selected from SEQ ID NO: 1 to 165 (Table 1) in the preparation of a medicament for the treatment of malignant neoplasia and breast cancer in particular.

Still another embodiment of the invention is a pharmaceutical composition which includes a reagent which specifically binds to a polynucleotide comprising a polynucleotide selected from SEQ ID NO: 1 to 165 (Table 1) or a polypeptide comprising a polypeptide selected from SEQ ID NO: 166 to 300, and a pharmaceutically acceptable carrier.

A further embodiment of the invention is a pharmaceutical composition comprising a polynucleotide including a sequence which hybridizes under stringent conditions to a polynucleotide comprising a polynucleotide selected from SEQ ID NO: 1 to 165 and encoding a polypeptide exhibiting the same biological function as given for the respective polynucleotide in Table 1 or 4, or encoding a polypeptide comprising a polypeptide selected from SEQ ID NO: 166 to 330. Pharmaceutical compositions, useful in the present invention may further include fusion proteins comprising a polypeptide comprising a polynucleotide selected from SEQ ID NO: 1 to 165, or a fragment thereof, antibodies, or antibody fragments

The invention also provides various kits. Such kit comprises reagents for assessing expression of a single or a plurality of genes selected from the marker genes listed in Table 1 or selected from the sub-set of genes listed in Table 2.

In one aspect, the invention provides a kit for assessing whether a patient is afflicted with breast cancer.

5 In another aspect, the invention provides a kit for assessing the suitability of each of a plurality of compounds for inhibiting a breast cancer in a patient. The kit comprises reagents for assessing expression of a marker gene listed within Table 1, or reagents for assessing the expression of each marker gene of a marker gene set listed in Table 2. The kit may also comprise a plurality of compounds.

10 In an additional aspect, the invention provides a kit for assessing the presence of breast cancer cells. This kit comprises an antibody, wherein the antibody binds specifically with a protein encoded by a marker gene listed within Table 1 or polypeptide fragment of the protein. The kit may also comprise a plurality of antibodies, wherein the plurality binds specifically with the protein encoded by each marker gene of a marker gene set listed in Table 2.

15 In yet another aspect, the invention provides a kit for assessing the presence of breast cancer cells, wherein the kit comprises a nucleic acid probe. The probe hybridizes specifically with a RNA transcript of a marker gene listed within Table 1 or cDNA of the transcript. The kit may also comprise a plurality of probes, wherein each of the probes hybridizes specifically with a RNA transcript of one of the marker genes of a marker gene set listed in Table 2.

20 It will be appreciated that the compositions, methods, and kits of the present invention may also include known cancer marker genes including known breast cancer marker genes. It will further be appreciated that the compositions, methods, and kits may be used to identify cancers other than breast cancer.

**DETAILED DESCRIPTION OF THE INVENTION****DEFINITIONS**

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"Differential expression", or "expression" as used herein, refers to both quantitative as well as qualitative differences in the genes' expression patterns depending on differential development, different genetic background of tumor cells and/or reaction to the tissue environment of the tumor. Differentially expressed genes may represent "marker genes," and/or "target genes". The expression pattern of a differentially expressed gene disclosed herein may be utilized as part of a prognostic or diagnostic breast cancer evaluation.

15

The term "pattern of expression" refers, e.g., to a determined level of gene expression compared either to a reference gene (e.g. housekeeper) or to a computed average expression value (e.g. in DNA-chip analyses). A pattern is not limited to the comparison of two genes but even more related to multiple comparisons of genes to a reference genes or samples. A certain "pattern of expression" may also result and be determined by comparison and measurement of several genes disclosed hereafter and display the relative abundance of these transcripts to each other.

20

Alternatively, a differentially expressed gene disclosed herein may be used in methods for identifying reagents and compounds and uses of these reagents and compounds for the treatment of breast cancer as well as methods of treatment. The differential regulation of the gene is not limited to a specific cancer cell type or clone, but rather displays the interplay of cancer cells, muscle cells, stromal cells, connective tissue cells, other epithelial cells, endothelial cells and blood vessels as well as cells of the immune system (e.g. lymphocytes, macrophages, killer cells).

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"Biological activity" or "bioactivity" or "activity" or "biological function", which are used interchangeably, herein mean an effector or antigenic function that is directly or

indirectly performed by a polypeptide (whether in its native or denatured conformation), or by any fragment thereof *in vivo* or *in vitro*. Biological activities include but are not limited to binding to polypeptides, binding to other proteins or molecules, enzymatic activity, signal transduction, activity as a DNA binding protein, as a transcription regulator, ability to bind damaged DNA, etc. A bioactivity  
5 can be modulated by directly affecting the subject polypeptide. Alternatively, a bioactivity can be altered by modulating the level of the polypeptide, such as by modulating expression of the corresponding gene.

10 The term "marker" or "biomarker" refers a biological molecule, e.g., a nucleic acid, peptide, hormone, etc., whose presence or concentration can be detected and correlated with a known condition, such as a disease state.

15 The term "marker gene," as used herein, refers to a differentially expressed gene which expression pattern may be utilized as part of predictive, prognostic or diagnostic process in malignant neoplasia or breast cancer evaluation, or which, alternatively, may be used in methods for identifying compounds useful for the treatment or prevention of malignant neoplasia and breast cancer in particular. A marker gene may also have the characteristics of a target gene.

20 "Target gene", as used herein, refers to a differentially expressed gene involved in breast cancer in a manner by which modulation of the level of target gene expression or of target gene product activity may act to ameliorate symptoms of malignant neoplasia and breast cancer in particular. A target gene may also have the  
25 characteristics of a marker gene.

30 The term "neoplastic lesion" or "neoplastic disease" or "neoplasia" refers to a cancerous tissue this includes carcinomas, (e.g., carcinoma in situ, invasive carcinoma, metastatic carcinoma) and pre-malignant conditions, neomorphic changes independent of their histological origin (e.g. ductal, lobular, medullary, mixed origin). The term "cancer" is not limited to any stage, grade, histomorphological

feature, invasiveness, aggressivity or malignancy of an affected tissue or cell aggregation. In particular stage 0 breast cancer, stage I breast cancer, stage II breast cancer, stage III breast cancer, stage IV breast cancer, grade I breast cancer, grade II breast cancer, grade III breast cancer, malignant breast cancer, primary carcinomas of the breast, and all other types of cancers, malignancies and transformations associated with the breast are included. The terms "neoplastic lesion" or "neoplastic disease" or "neoplasia" or "cancer" are not limited to any tissue or cell type they also include primary, secondary or metastatic lesion of cancer patients, and also comprises lymphnodes affected by cancer cells or minimal residual disease cells either locally deposited (e.g. bone marrow, liver, kidney) or freely floating throughout the patients body.

Furthermore, the term "characterizing the state of a neoplastic disease" is related to, but not limited to, measurements and assessment of one or more of the following conditions: Type of tumor, histomorphological appearance, dependence on external signal (e.g. hormones, growth factors), invasiveness, motility, state by TNM (Lit. 2) or similar, aggressivity, malignancy, metastatic potential, and responsiveness to a given therapy.

The term "biological sample", as used herein, refers to a sample obtained from an organism or from components (e.g., cells) of an organism. The sample may be of any biological tissue or fluid. Frequently the sample will be a "clinical sample" which is a sample derived from a patient. Such samples include, but are not limited to, sputum, blood, blood cells (e.g., white cells), tissue or fine needle biopsy samples, cell-containing bodyfluids, free floating nucleic acids, urine, peritoneal fluid, and pleural fluid, or cells therefrom. Biological samples may also include sections of tissues such as frozen or fixed sections taken for histological purposes. A biological sample to be analyzed is tissue material from neoplastic lesion taken by aspiration or punctuation, excision or by any other surgical method leading to biopsy or resected cellular material. Such biological sample may comprises cells obtained from a patient. The cells may be found in a breast cell "smear" collected, for example, by a



nipple aspiration, ductal lavage, fine needle biopsy or from provoked or spontaneous nipple discharge. In another embodiment, the sample is a body fluid. Such fluids include, for example, blood fluids, lymph, ascitic fluids, gynecological fluids, or urine but not limited to these fluids.

5

The term "therapy modality", "therapy mode", "regimen" or "chemo regimen" as well as "therapy regime" refers to a timely sequential or simultaneous administration of anti tumor, and/or immune stimulating, and/or blood cell proliferative agents, and/or radiation therapy, and/or hyperthermia, and/or hypothermia for cancer therapy.

10 The administration of these can be performed in an adjuvant and/or neoadjuvant mode. The composition of such "protocol" may vary in dose of the single agent, timeframe of application and frequency of administration within a defined therapy window. Currently various combinations of various drugs and/or physical methods, and various schedules are under investigation.

15

By "array" or "matrix" is meant an arrangement of addressable locations or "addresses" on a device. The locations can be arranged in two dimensional arrays, three dimensional arrays, or other matrix formats. The number of locations can range from several to at least hundreds of thousands. Most importantly, each location represents a totally independent reaction site. Arrays include but are not limited to nucleic acid arrays, protein arrays and antibody arrays. A "nucleic acid array" refers to an array containing nucleic acid probes, such as oligonucleotides, polynucleotides or larger portions of genes. The nucleic acid on the array is preferably single stranded. Arrays wherein the probes are oligonucleotides are referred to as "oligonucleotide arrays" or "oligonucleotide chips." A "microarray," herein also refers to a "biochip" or "biological chip", an array of regions having a density of discrete regions of at least about 100/cm<sup>2</sup>, and preferably at least about 1000/cm<sup>2</sup>. The regions in a microarray have typical dimensions, e.g., diameters, in the range of between about 10-250  $\mu$ m, and are separated from other regions in the array by about the same distance. A "protein array" refers to an array containing polypeptide probes or protein probes which can be in native form or denatured. An "antibody array"

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refers to an array containing antibodies which include but are not limited to monoclonal antibodies (e.g. from a mouse), chimeric antibodies, humanized antibodies or phage antibodies and single chain antibodies as well as fragments from antibodies.

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The term "agonist", as used herein, is meant to refer to an agent that mimics or upregulates (e.g., potentiates or supplements) the bioactivity of a protein. An agonist can be a wild-type protein or derivative thereof having at least one bioactivity of the wild-type protein. An agonist can also be a compound that upregulates expression of a gene or which increases at least one bioactivity of a protein. An agonist can also be a compound which increases the interaction of a polypeptide with another molecule, e.g., a target peptide or nucleic acid.

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The term "antagonist" as used herein is meant to refer to an agent that downregulates (e.g., suppresses or inhibits) at least one bioactivity of a protein. An antagonist can be a compound which inhibits or decreases the interaction between a protein and another molecule, e.g., a target peptide, a ligand or an enzyme substrate. An antagonist can also be a compound that downregulates expression of a gene or which reduces the amount of expressed protein present.

15

20

"Small molecule" as used herein, is meant to refer to a composition, which has a molecular weight of less than about 5 kD and most preferably less than about 4 kD. Small molecules can be nucleic acids, peptides, polypeptides, peptidomimetics, carbohydrates, lipids or other organic (carbon-containing) or inorganic molecules. Many pharmaceutical companies have extensive libraries of chemical and/or biological mixtures, often fungal, bacterial, or algal extracts, which can be screened with any of the assays of the invention to identify compounds that modulate a bioactivity.

25

The terms "modulated" or "modulation" or "regulated" or "regulation" and "differentially regulated" as used herein refer to both upregulation (i.e., activation or

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stimulation (e.g., by agonizing or potentiating) and down regulation [i.e., inhibition or suppression (e.g., by antagonizing, decreasing or inhibiting)].

5 "Transcriptional regulatory unit" refers to DNA sequences, such as initiation signals, enhancers, and promoters, which induce or control transcription of protein coding sequences with which they are operably linked. In preferred embodiments, transcription of one of the genes is under the control of a promoter sequence (or other transcriptional regulatory sequence) which controls the expression of the recombinant gene in a cell-type in which expression is intended. It will also be  
10 understood that the recombinant gene can be under the control of transcriptional regulatory sequences which are the same or which are different from those sequences which control transcription of the naturally occurring forms of the polypeptide.

15 The term "derivative" refers to the chemical modification of a polypeptide sequence, or a polynucleotide sequence. Chemical modifications of a polynucleotide sequence can include, for example, replacement of hydrogen by an alkyl, acyl, or amino group. A derivative polynucleotide encodes a polypeptide which retains at least one biological or immunological function of the natural molecule. A derivative polypeptide is one modified by glycosylation, pegylation, or any similar process that  
20 retains at least one biological or immunological function of the polypeptide from which it was derived.

25 The term "nucleotide analog" refers to oligomers or polymers being at least in one feature different from naturally occurring nucleotides, oligonucleotides or polynucleotides, but exhibiting functional features of the respective naturally occurring nucleotides (e.g. base pairing, hybridization, coding information) and that can be used for said compositions. The nucleotide analogs can consist of non-naturally occurring bases or polymer backbones, examples of which are LNAs, PNAs and Morpholinos. The nucleotide analog has at least one molecule different from its naturally occurring  
30 counterpart or equivalent.

"BREAST CANCER GENES" or "BREAST CANCER GENE" as used herein refers to the polynucleotides of SEQ ID NO:1 to 165 (listed in Table 1), as well as derivatives, fragments, analogs and homologues thereof, the polypeptides encoded thereby, (SEQ ID NO:166 to 330, see Table1) as well as derivatives, fragments, analogs and homologues thereof and the corresponding genomic transcription units which can be derived or identified with standard techniques well known in the art using the information disclosed in Tables 1 to 5. The Genename, Reference Sequence, unique Gene-identifier, and the Locuslink ID numbers of the polynucleotide sequences of the SEQ ID NO: 1 to 65 and the polypeptides of the SEQ ID NO: 166 to 330 are shown in Table 1, the gene description, gene function and subcellular localization is given in Tables 4.

The term "chromosomal region" as used herein refers to a consecutive DNA stretch on a chromosome which can be defined by cytogenetic or other genetic markers such as e.g. restriction length polymorphisms (RFLPs), single nucleotide polymorphisms (SNPs), expressed sequence tags (ESTs), sequence tagged sites (STSs), microsatellites, variable number of tandem repeats (VNTRs) and genes. Typically a chromosomal region consists of up to 2 Megabases (MB), up to 4 MB, up to 6 MB, up to 8 MB, up to 10 MB, up to 20 MB or even more MB.

The term "kit" as used herein refers to any manufacture (e.g. a diagnostic or research product) comprising at least one reagent, e.g. a probe, for specifically detecting the expression of at least one marker gene disclosed in the invention, in particular of those genes listed in Table 2, whereas the manufacture is being sold, distributed, and/or promoted as a unit for performing the methods of the present invention. The genes, primer and probes listed in Table 2 and 5 or any combination of at least two of them, regard as one single test for the purposes, methods and disclosures of this invention. Also reagents (e.g. immunoassays) to detect the presence, the stability, activity, complexity of the respective marker gene products comprising polypeptides selected from SEQ ID NO:166 to 330 regard as components of the kit. In addition,

any combination of nucleic acid and protein detection as disclosed in the invention are regard as a kit.

5 The present invention provides polynucleotide sequences and proteins encoded thereby, as well as probes derived from the polynucleotide sequences, antibodies directed to the encoded proteins, and predictive, preventive, diagnostic, prognostic and therapeutic uses for individuals which are at risk for or which have malignant neoplasia and breast cancer in particular. The sequences disclosure herein have been found to be differentially expressed in samples from breast cancer.

10 The present invention is based on the identification of 165 genes that are differentially regulated (up- or down regulated) in tumor biopsies of patients with clinical evidence of breast cancer.. The characterization of the co-expression of some of these genes provides newly identified roles in breast cancer. The gene names, the database accession numbers (Genename, Reference Sequence, unique Gene-  
15 identifier, and the Locuslink ID numbers) as well as the putative or known functions of the encoded proteins and their subcellular localization are given in Tables 1 to 4. The primer sequences used for the gene amplification and hybridization probes are shown in Table 5.

20

The present invention relates to:

1. A method for characterizing the state of a neoplastic disease in a subject, comprising  
25 (i) determining the pattern of expression levels of at least 6, 8, 10, 15, 20, 30, or 47 marker genes, comprised in a group of marker genes consisting of SEQ ID NO:1 to 165, in a biological sample from said subject,  
30 (ii) comparing the pattern of expression levels determined in (i) with one or several reference pattern(s) of expression levels,

- (iii) characterizing the state of said neoplastic disease in said subject from the outcome of the comparison in step (ii).

2. A method for detection, diagnosis, screening, monitoring, and/or prognosis of a neoplastic disease in a subject, comprising

- (i) determining the pattern of expression levels of at least 1, 2, 3, 5, 10, 15, 20, 30, or 47 marker genes, comprised in a group of marker genes consisting of SEQ ID NOs: 1 to 17, 19 to 33, 35 to 50, 52 to 64, 66 to 85, 88 to 91, and 93 to 165 in biological samples from said subject,
- (ii) comparing the pattern of expression levels determined in (i) with one or several reference pattern(s) of expression levels,
- (iii) detecting, diagnosing, screening, monitoring, and/or prognosing said neoplastic disease in said subject from the outcome of the comparison in step (ii).

Determination of an expression level can comprise a quantification of the expression level and/or a purely qualitative determination of the expression level.

A "pattern of expression levels" of a single gene is to be understood as the expression level of said gene as determined by suitable methods.

Nucleic acid molecules, referred to with a specific SEQ ID NO, within the meaning of the invention, are to be understood as comprising also variants of said nucleic acid molecules, which can be derived from the original nucleic acid molecules by deletion, insertion or transposition of nucleotides, provided said variants still have an 80, 90, 95, or 99% sequence identity towards the original sequence. Preferably the variants still have the same biological activity and/or function as have the original molecules.

It is obvious to the person skilled in the art that a reference to a nucleotide sequence is meant to comprise the reference to the associated protein sequence which is coded by said nucleotide sequence.

- 5        "% identity" of a first sequence towards a second sequence, within the meaning of the invention, means the % identity which is calculated as follows: First the optimal global alignment between the two sequences is determined with the CLUSTALW algorithm [Thomson JD, Higgins DG, Gibson TJ. 1994. ClustalW: Improving the sensitivity of progressive multiple sequence alignment through sequence weighting, positions-specific gap penalties and weight matrix choice. Nucleic Acids Res., 22: 10        4673-4680], Version 1.8, applying the following command line syntax: ./clustalw -infile=./infile.txt        -output=        -outorder=aligned        -pwmatrix=gonnet -pwndnamatrix=clustalw        -pwgapopen=10.0        -pwgapext=0.1        -matrix=gonnet -gapopen=10.0 -gapext=0.05 -gapdist=8 -hgapresidues=GPSNDQERK -maxdiv=40.
- 15        Implementations of the CLUSTAL W algorithm are readily available at numerous sites on the internet, including, e.g., <http://www.ebi.ac.uk>. Thereafter, the number of matches in the alignment is determined by counting the number of identical nucleotides (or amino acid residues) in aligned positions. Finally, the total number of matches is divided by the number of nucleotides (or amino acid residues) of the 20        longer of the two sequences, and multiplied by 100 to yield the % identity of the first sequence towards the second sequence.
- 25        3.        A method of count 1 or 2, wherein said method comprises multiple determinations of a pattern of expression levels, at different points in time, thereby allowing to monitor the development of said neoplastic disease in said subject.
- 30        4.        A method of count 1, wherein said method comprises an estimation of the likelihood of success of a given mode of treatment for said neoplastic disease in said subject.

5. A method of count 1, wherein said method comprises an assessment of whether the subject is expected to respond or whether the subject is expected not to a given mode of treatment for said neoplastic disease.

5 The terms "to respond" or "not to respond" are to be understood in a qualitative and/or in a quantitative fashion. "To respond" and "not to respond" is to be assessed with regard to a suitable reference responses, such as, e.g., responses shown by "responders" and "not-responders" to a certain mode of treatment or modality of treatment.

10

6. A method of count 4 or 5, wherein a predictive algorithm is used.

Predictive algorithms, which are well known to a person skilled in the art of data analysis, are to be understood as being any kind of predictive algorithm known in the art. Preferred examples of such algorithms are, e.g., the SVM algorithm disclosed in

15 Example 4.

7. A method of count 6, wherein the predictive algorithm is a Support Vector Machine.

20

Support Vector Machines are algorithms, well known to the person skilled in the art of data analysis. A Support Vector Machine algorithm is disclosed in Example 4.

8. A method of any of counts 4 to 7, wherein said given mode of treatment

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- (i) acts on cell proliferation, and/or
- (ii) acts on cell survival, and/or
- (iii) acts on cell motility, and/or
- (iv) is an anthracycline based mode of treatment, and/or
- 30 (v) comprises administration of epirubicin and/or cyclophosphamid.



9. A method of treatment for a subject afflicted with a neoplastic disease, comprising
- 5 (i) identifying a promising mode of treatment with the method of count 4 or 5,
- (ii) treating said neoplastic disease in said patient by the mode of treatment identified in step (i).
10. A method of screening for subjects afflicted with a neoplastic disease, wherein the method of count 1 or 2 is applied to a plurality of subjects.
11. A method of screening for substances and/or therapy modalities having curative effect on a neoplastic disease comprising
- 15 (i) obtaining a biological sample from a subject afflicted with said neoplastic disease,
- (ii) assessing, from said biological sample, using the method of count 4 or 5, whether said subject is expected to respond to a given mode of treatment for said neoplastic disease,
- 20 (iii) if said subject is expected to respond to said given mode of treatment, incubating said biological sample with said substance under said therapy modalities,
- (iv) observing changes in said biological sample triggered by said test substance under said therapy modalities,
- 25 (v) selecting or rejecting said test substance and/or said therapy modalities, based on the observation of changes in said biological sample under (iv).
- 30 Selecting specific biological samples of, e.g., good responders to a given therapy can help to identify novel substances and/or therapy modalities for the treatment of said specific neoplastic disease.

12. A method of screening for compounds having curative effect on a neoplastic disease comprising

- 5 (i) incubating biological samples or extracts of these with a test substance,
- (ii) determining the pattern of expression levels of at least 1, 2, 3, 5, 10, 15, 20, 30, or 47 marker genes, comprised in a group of marker genes consisting of SEQ ID NO:1 to 17, 19 to 33, 35 to 50, 52 to 64, 66 to 10 85, 88 to 91, and 93 to 165 in said biological sample,
- (iii) comparing the pattern of expression levels determined in (ii) with one or several reference pattern(s),
- (iv) selecting or rejecting said test substance, based on the comparison performed under (iii).

15

13. A method of any of counts 1 to 12 wherein said marker genes are comprised in a group of marker genes listed in Table 2.

20 Marker genes listed in Table 2 are shown to be particularly informative with respect to assessing the propability of success of a certain mode of treatment for a given neoplastic disease. Marker genes of Table 2 are preferred marker genes, according to the invention.

14. A method of any of counts 1 to 13, wherein the expression level is determined

25

- (i) with a hybridization based method, or
- (ii) with a hybridization based method utilizing arrayed probes, or
- (iii) with a hybridization based method utilizing individually labeled probes, or
- 30 (iv) by real time real time PCR, or

- (v) by assessing the expression of polypeptides, proteins or derivatives thereof, or
- (vi) by assessing the amount of polypeptides, proteins or derivatives thereof.
- 5
15. A method of any of counts 1 to 14, wherein the neoplastic disease is breast cancer.
- 10
16. A kit comprising at least 6, 8, 10, 15, 20, 30, or 47 primer pairs and probes suitable for marker genes comprised in a group of marker genes consisting of
- (i) SEQ ID NO:1 to SEQ ID NO:165, or
- (ii) the marker genes listed in Table 2.
- 15
17. A kit comprising at least 6, 8, 10, 15, 20, 30, or 47 sets of individually labeled probes, each having a sequence comprised in a group of sequences consisting of SEQ ID NO:331 to SEQ ID NO:471.
- 20
18. A kit comprising at least 6, 8, 10, 15, 20, 30, or 47 sets of arrayed probes, each having a sequence comprised in a group of sequences consisting of SEQ ID NO:331 to SEQ ID NO:471.

Biological relevance of the genes which are part of the invention

- 25
- Some of the genes listed in Table 1 represent biological, cellular processes and are characterized by similar regulation of genes. By the way of illustration but limited to the following examples a few characteristic genes from Table 1 are described in later by greater detail:

## MAD2L1

The initiation of chromosome segregation at anaphase is linked by the spindle assembly checkpoint to the completion of chromosome-microtubule attachment during metaphase. To determine the function of the Mad2 protein during normal cell division, knock out experiments in mice were performed. These cells were unable to arrest in response to spindle disruption. At embryonic day 6.5, the cells of the epiblast began rapid cell division, and the absence of a checkpoint resulted in widespread chromosome missegregation and apoptosis. In contrast, the postmitotic trophoblast giant cells survived without Mad2. Thus, the spindle assembly checkpoint is required for accurate chromosome segregation in mitotic mouse cells and for embryonic viability, even in the absence of spindle damage.

Meiosis I nondisjunction in spindle checkpoint mutants could be prevented by delaying the onset of anaphase. In a recombinant-defective mutant, the checkpoint delayed the biochemical events of anaphase I, suggesting that chromosomes that are attached to microtubules but are not under tension can activate the spindle checkpoint. Spindle checkpoint mutants reduced the accuracy of chromosome segregation in meiosis I much more than that in meiosis II, suggesting that checkpoint defects may contribute to Down syndrome and possibly to the "chaotic" polyploidy observed in cancer.

## IGFBP4

Seven structurally distinct insulin-like growth factor binding proteins have been isolated and their cDNAs cloned: IGFBP1, IGFBP2, IGFBP3, IGFBP4, IGFBP5, IGFBP6, and IGFBP7. The proteins display strong sequence homologies, suggesting that they are encoded by a closely related family of genes. The IGFBPs contain 3 structurally distinct domains each comprising approximately one-third of the molecule. The N-terminal domain 1 and the C-terminal domain 3 of the 6 human IGFBPs show moderate to high levels of sequence identity including 12 and 6

invariant cysteine residues in domains 1 and 3, respectively (IGFBP6 contains 10 cysteine residues in domain 1), and are thought to be the IGF binding domains. Domain 2 is defined primarily by a lack of sequence identity among the 6 IGFBPs and by a lack of cysteine residues, though it does contain 2 cysteines in IGFBP4. Domain 3 is homologous to the thyroglobulin type I repeat unit. Studies suggested that the primary effect of the proteins is the attenuation of IGF activity and suggested that they contribute to the control of IGF-mediated cell growth and metabolism

#### DDB2

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In human cells, efficient global genomic repair of DNA damage induced by ultraviolet radiation requires the p53 tumor suppressor. The p48 gene is required for expression of an ultraviolet radiation-damaged DNA-binding activity and is disrupted by mutations in the subset of xeroderma pigmentosum group E cells that lack this activity, DDB-negative XPE. p48 mRNA levels are strongly depend on basal p53 expression and increase further after DNA damage in a p53-dependent manner. Furthermore, like p53  $-/-$  cells, xeroderma pigmentosum group E cells are deficient in global genomic repair. These results identified p48 as a link between p53 and the nucleotide excision-repair apparatus.

20

UV-damaged DNA-binding activity (UV-DDB) is deficient in cell lines and primary tissues from rodents. Transfection of p48 conferred UV-DDB to hamster cells and enhanced removal of cyclobutane pyrimidine dimers (CPDs) from genomic DNA and from the nontranscribed strand of an expressed gene. Expression of p48 suppressed UV-induced mutations arising from the nontranscribed strand but had no effect on cellular UV sensitivity. The results defined the role of p48 in DNA repair, demonstrated the importance of CPDs in mutagenesis, and suggested how rodent models can be improved to better reflect cancer susceptibility in humans.

25

## HSPA2

Several heat-shock protein genes are located in the major histocompatibility complex on chromosome 6, e.g., HSPA1 . However HSPA2 is located on 14q22-q24 . isolated  
5 The clone for HSPA2 is characterized by a single open reading frame of 1,917 basepairs that encodes a 639-amino acid protein with a predicted molecular weight of 70,030 Da. Analysis of the sequence indicated that HSPA2 is the human homolog of the murine Hsp70-2 gene with 91.7% identity in the nucleotide coding sequence and 98.2% in the corresponding amino acid sequence. HSPA2 has less amino acid  
10 homology to the other members of the human HSP70 gene family. HSPA2 is constitutively expressed in most tissues, with very high levels in testis and skeletal muscle. HSPA2 is expressed abundantly in muscle, heart, esophagus, and brain, and to a lesser extent in testis. A female homozygous knockout mice for Hsp70-2 undergo normal meiosis and is fertile. In contrast, homozygous male knockout mice  
15 lacked postmeiotic spermatids and mature sperm and were infertile. Hsp70-2 is normally associated with synaptonemal complexes in the nuclei of meiotic spermatocytes. In the male knockouts, these structures were abnormal by late prophase. One can observe also a large increase in spermatocyte apoptosis.

20 Polynucleotides

A „BREAST CANCER GENE“ polynucleotide can be single- or double-stranded and comprises a coding sequence or the complement of a coding sequence for a „BREAST CANCER GENE“ polypeptide. Degenerate nucleotide sequences  
25 encoding human „BREAST CANCER GENE“ polypeptides, as well as homologous nucleotide sequences which are at least about 50, 55, 60, 65, 70, preferably about 75, 90, 96, or 98% identical to the nucleotide sequences of SEQ ID NO: 1 to 165 also are „BREAST CANCER GENE“ polynucleotides. Percent sequence identity between the sequences of two polynucleotides is determined using computer programs such as  
30 ALIGN which employ the FASTA algorithm, using an affine gap search with a gap open penalty of -12 and a gap extension penalty of -2. Complementary DNA (cDNA)

molecules, species homologues, and variants of „BREAST CANCER GENE“ polynucleotides which encode biologically active „BREAST CANCER GENE“ polypeptides also are „BREAST CANCER GENE“ polynucleotides.

5     Preparation of Polynucleotides

10     A naturally occurring „BREAST CANCER GENE“ polynucleotide can be isolated free of other cellular components such as membrane components, proteins, and lipids. Polynucleotides can be made by a cell and isolated using standard nucleic acid purification techniques, or synthesized using an amplification technique, such as the polymerase chain reaction (PCR), or by using an automatic synthesizer. Methods for isolating polynucleotides are routine and are known in the art. Any such technique for obtaining a polynucleotide can be used to obtain isolated „BREAST CANCER GENE“ polynucleotides. For example, restriction enzymes and probes can be used to  
15     isolate polynucleotide fragments which comprises „BREAST CANCER GENE“ nucleotide sequences. Isolated polynucleotides are in preparations which are free or at least 70, 80, or 90% free of other molecules.

20     „BREAST CANCER GENE“ cDNA molecules can be made with standard molecular biology techniques, using „BREAST CANCER GENE“ mRNA as a template. Any RNA isolation technique which does not select against the isolation of mRNA may be utilized for the purification of such RNA samples. See, for example, Sambrook et al., 1989, (6); and Ausubel, F. M. et al., 1989, (7), both of which are incorporated herein by reference in their entirety. Additionally, large numbers of tissue samples  
25     may readily be processed using techniques well known to those of skill in the art, such as, for example, the single-step RNA isolation process of Chomczynski, P. (1989, U.S. Pat. No. 4,843,155), which is incorporated herein by reference in its entirety.

30     „BREAST CANCER GENE“ cDNA molecules can thereafter be replicated using molecular biology techniques known in the art and disclosed in manuals such as

Sambrook et al., 1989, (6) . An amplification technique, such as PCR, can be used to obtain additional copies of polynucleotides of the invention, using either human genomic DNA or cDNA as a template.

5 Alternatively, synthetic chemistry techniques can be used to synthesize „BREAST CANCER GENE“ polynucleotides. The degeneracy of the genetic code allows alternate nucleotide sequences to be synthesized which will encode a „BREAST CANCER GENE“ polypeptide or a biologically active variant thereof.

10 Identification of differential expression

Transcripts within the collected RNA samples which represent RNA produced by differentially expressed genes may be identified by utilizing a variety of methods which are well known to those of skill in the art. For example, differential screening  
15 [Tedder, T. F. et al., 1988, (8)], subtractive hybridization [Hedrick, S. M. et al., 1984, (9); Lee, S. W. et al., 1984, (10)], and, preferably, differential display (Liang, P., and Pardee, A. B., 1993, U.S. Pat. No. 5,262,311, which is incorporated herein by reference in its entirety), may be utilized to identify polynucleotide sequences derived from genes that are differentially expressed.

20 Differential screening involves the duplicate screening of a cDNA library in which one copy of the library is screened with a total cell cDNA probe corresponding to the mRNA population of one cell type while a duplicate copy of the cDNA library is screened with a total cDNA probe corresponding to the mRNA population of a  
25 second cell type. For example, one cDNA probe may correspond to a total cell cDNA probe of a cell type derived from a control subject, while the second cDNA probe may correspond to a total cell cDNA probe of the same cell type derived from an experimental subject. Those clones which hybridize to one probe but not to the other potentially represent clones derived from genes differentially expressed in the cell  
30 type of interest in control versus experimental subjects.



Subtractive hybridization techniques generally involve the isolation of mRNA taken from two different sources, e.g., control and experimental tissue, the hybridization of the mRNA or single-stranded cDNA reverse-transcribed from the isolated mRNA, and the removal of all hybridized, and therefore double-stranded, sequences. The remaining non-hybridized, single-stranded cDNAs, potentially represent clones derived from genes that are differentially expressed in the two mRNA sources. Such single-stranded cDNAs are then used as the starting material for the construction of a library comprising clones derived from differentially expressed genes.

The differential display technique describes a procedure, utilizing the well known polymerase chain reaction (PCR; the experimental embodiment set forth in Mullis, K. B., 1987, U.S. Pat. No. 4,683,202) which allows for the identification of sequences derived from genes which are differentially expressed. First, isolated RNA is reverse-transcribed into single-stranded cDNA, utilizing standard techniques which are well known to those of skill in the art. Primers for the reverse transcriptase reaction may include, but are not limited to, oligo dT-containing primers, preferably of the reverse primer type of oligonucleotide described below. Next, this technique uses pairs of PCR primers, as described below, which allow for the amplification of clones representing a random subset of the RNA transcripts present within any given cell. Utilizing different pairs of primers allows each of the mRNA transcripts present in a cell to be amplified. Among such amplified transcripts may be identified those which have been produced from differentially expressed genes.

The reverse oligonucleotide primer of the primer pairs may contain an oligo dT stretch of nucleotides, preferably eleven nucleotides long, at its 5' end, which hybridizes to the poly(A) tail of mRNA or to the complement of a cDNA reverse transcribed from an mRNA poly(A) tail. Second, in order to increase the specificity of the reverse primer, the primer may contain one or more, preferably two, additional nucleotides at its 3' end. Because, statistically, only a subset of the mRNA derived sequences present in the sample of interest will hybridize to such primers, the additional nucleotides allow the primers to amplify only a subset of the mRNA

derived sequences present in the sample of interest. This is preferred in that it allows more accurate and complete visualization and characterization of each of the bands representing amplified sequences.

5 The forward primer may contain a nucleotide sequence expected, statistically, to have the ability to hybridize to cDNA sequences derived from the tissues of interest. The nucleotide sequence may be an arbitrary one, and the length of the forward oligonucleotide primer may range from about 9 to about 13 nucleotides, with about 10 nucleotides being preferred. Arbitrary primer sequences cause the lengths of the  
10 amplified partial cDNAs produced to be variable, thus allowing different clones to be separated by using standard denaturing sequencing gel electrophoresis. PCR reaction conditions should be chosen which optimize amplified product yield and specificity, and, additionally, produce amplified products of lengths which may be resolved utilizing standard gel electrophoresis techniques. Such reaction conditions are well  
15 known to those of skill in the art, and important reaction parameters include, for example, length and nucleotide sequence of oligonucleotide primers as discussed above, and annealing and elongation step temperatures and reaction times. The pattern of clones resulting from the reverse transcription and amplification of the mRNA of two different cell types is displayed via sequencing gel electrophoresis and  
20 compared. Differences in the two banding patterns indicate potentially differentially expressed genes.

When screening for full-length cDNAs, it is preferable to use libraries that have been size-selected to include larger cDNAs. Randomly-primed libraries are preferable, in  
25 that they will contain more sequences which contain the 5' regions of genes. Use of a randomly primed library may be especially preferable for situations in which an oligo d(T) library does not yield a full-length cDNA. Genomic libraries can be useful for extension of sequence into 5' nontranscribed regulatory regions.

30 Commercially available capillary electrophoresis systems can be used to analyze the size or confirm the nucleotide sequence of PCR or sequencing products. For

example, capillary sequencing can employ flowable polymers for electrophoretic separation, four different fluorescent dyes (one for each nucleotide) which are laser activated, and detection of the emitted wavelengths by a charge coupled device camera. Output/light intensity can be converted to electrical signal using appropriate software (e.g. GENOTYPER and Sequence NAVIGATOR, Perkin Elmer; ABI), and the entire process from loading of samples to computer analysis and electronic data display can be computer controlled. Capillary electrophoresis is especially preferable for the sequencing of small pieces of DNA which might be present in limited amounts in a particular sample.

Once potentially differentially expressed gene sequences have been identified via bulk techniques such as, for example, those described above, the differential expression of such putatively differentially expressed genes should be corroborated. Corroboration may be accomplished via, for example, such well known techniques as Northern analysis and/or RT-PCR. Upon corroboration, the differentially expressed genes may be further characterized, and may be identified as target and/or marker genes, as discussed, below.

Also, amplified sequences of differentially expressed genes obtained through, for example, differential display may be used to isolate full length clones of the corresponding gene. The full length coding portion of the gene may readily be isolated, without undue experimentation, by molecular biological techniques well known in the art. For example, the isolated differentially expressed amplified fragment may be labeled and used to screen a cDNA library. Alternatively, the labeled fragment may be used to screen a genomic library.

An analysis of the tissue distribution of the mRNA produced by the identified genes may be conducted, utilizing standard techniques well known to those of skill in the art. Such techniques may include, for example, Northern analyses and RT-PCR. Such analyses provide information as to whether the identified genes are expressed in tissues expected to contribute to breast cancer. Such analyses may also provide

quantitative information regarding steady state mRNA regulation, yielding data concerning which of the identified genes exhibits a high level of regulation in, preferably, tissues which may be expected to contribute to breast cancer.

5 Such analyses may also be performed on an isolated cell population of a particular cell type derived from a given tissue. Additionally, standard in situ hybridization techniques may be utilized to provide information regarding which cells within a given tissue express the identified gene. Such analyses may provide information regarding the biological function of an identified gene relative to breast cancer in  
10 instances wherein only a subset of the cells within the tissue is thought to be relevant to breast cancer.

Extending Polynucleotides

15 In one embodiment of such a procedure for the identification and cloning of full length gene sequences, RNA may be isolated, following standard procedures, from an appropriate tissue or cellular source. A reverse transcription reaction may then be performed on the RNA using an oligonucleotide primer complimentary to the mRNA that corresponds to the amplified fragment, for the priming of first strand synthesis.  
20 Because the primer is anti-parallel to the mRNA, extension will proceed toward the 5' end of the mRNA. The resulting RNA hybrid may then be "tailed" with guanines using a standard terminal transferase reaction, the hybrid may be digested with RNase H, and second strand synthesis may then be primed with a poly-C primer. Using the two primers, the 5' portion of the gene is amplified using PCR. Sequences  
25 obtained may then be isolated and recombined with previously isolated sequences to generate a full-length cDNA of the differentially expressed genes of the invention. For a review of cloning strategies and recombinant DNA techniques, see e.g., Sambrook et al., (6); and Ausubel et al., (7).

30 Various PCR-based methods can be used to extend the polynucleotide sequences disclosed herein to detect upstream sequences such as promoters and regulatory

elements. For example, restriction site PCR uses universal primers to retrieve unknown sequence adjacent to a known locus [Sarkar, 1993, (11)]. Genomic DNA is first amplified in the presence of a primer to a linker sequence and a primer specific to the known region. The amplified sequences are then subjected to a second round of PCR with the same linker primer and another specific primer internal to the first one. Products of each round of PCR are transcribed with an appropriate RNA polymerase and sequenced using reverse transcriptase.

Inverse PCR also can be used to amplify or extend sequences using divergent primers based on a known region [Triglia et al., 1988, (12)]. Primers can be designed using commercially available software, such as OLIGO 4.06 Primer Analysis software (National Biosciences Inc., Plymouth, Minn.), to be e.g. 2230 nucleotides in length, to have a GC content of 50% or more, and to anneal to the target sequence at temperatures about 68-72°C. The method uses several restriction enzymes to generate a suitable fragment in the known region of a gene. The fragment is then circularized by intramolecular ligation and used as a PCR template.

Another method which can be used is capture PCR, which involves PCR amplification of DNA fragments adjacent to a known sequence in human and yeast artificial chromosome DNA [Lagerstrom et al., 1991, (13)]. In this method, multiple restriction enzyme digestions and ligations also can be used to place an engineered double-stranded sequence into an unknown fragment of the DNA molecule before performing PCR.

Additionally, PCR, nested primers, and PROMOTERFINDER libraries (CLONTECH, Palo Alto, Calif.) can be used to walk genomic DNA (CLONTECH, Palo Alto, Calif.). This process avoids the need to screen libraries and is useful in finding intron/exon junctions.

The sequences of the identified genes may be used, utilizing standard techniques, to place the genes onto genetic maps, e.g., mouse [Copeland & Jenkins, 1991, (14)] and

human genetic maps [Cohen, et al., 1993 ,(15)]. Such mapping information may yield information regarding the genes' importance to human disease by, for example, identifying genes which map near genetic regions to which known genetic breast cancer tendencies map.

5

Identification of Polynucleotide Variants and Homologues or splice Variants

Variants and homologues of the „BREAST CANCER GENE“ polynucleotides described above also are „BREAST CANCER GENE“ polynucleotides. Typically, homologous „BREAST CANCER GENE“ polynucleotide sequences can be identified by hybridization of candidate polynucleotides to known „BREAST CANCER GENE“ polynucleotides under stringent conditions, as is known in the art. For example, using the following wash conditions: 2X SSC (0.3 M NaCl, 0.03 M sodium citrate, pH 7.0), 0.1% SDS, room temperature twice, 30 minutes each; then 2X SSC, 0.1% SDS, 50 EC once, 30 minutes; then 2X SSC, room temperature twice, 10 minutes each homologous sequences can be identified which contain at most about 25-30% basepair mismatches. More preferably, homologous polynucleotide strands contain 15-25% basepair mismatches, even more preferably 5-15% basepair mismatches.

20

Species homologues of the „BREAST CANCER GENE“ polynucleotides disclosed herein also can be identified by making suitable probes or primers and screening cDNA expression libraries from other species, such as mice, monkeys, or yeast. Human variants of „BREAST CANCER GENE“ polynucleotides can be identified, for example, by screening human cDNA expression libraries. It is well known that the  $T_m$  of a double-stranded DNA decreases by 1-1.5°C with every 1% decrease in homology [Bonner et al., 1973, (16)]. Variants of human „BREAST CANCER GENE“ polynucleotides or „BREAST CANCER GENE“ polynucleotides of other species can therefore be identified by hybridizing a putative homologous „BREAST CANCER GENE“ polynucleotide with a polynucleotide having a nucleotide sequence of one of the sequences of the SEQ ID NO: 1 to 165 or the complement

30

thereof to form a test hybrid. The melting temperature of the test hybrid is compared with the melting temperature of a hybrid comprising polynucleotides having perfectly complementary nucleotide sequences, and the number or percent of basepair mismatches within the test hybrid is calculated.

5

Nucleotide sequences which hybridize to „BREAST CANCER GENE“ polynucleotides or their complements following stringent hybridization and/or wash conditions also are „BREAST CANCER GENE“ polynucleotides. Stringent wash conditions are well known and understood in the art and are disclosed, for example, in Sambrook et al., (6). Typically, for stringent hybridization conditions a combination of temperature and salt concentration should be chosen that is approximately 12to20°C below the calculated  $T_m$  of the hybrid under study. The  $T_m$  of a hybrid between a „BREAST CANCER GENE“ polynucleotide having a nucleotide sequence of one of the sequences of the SEQ ID NO: 1to165 or the complement thereof and a polynucleotide sequence which is at least about 50, preferably about 75, 90, 96, or 98% identical to one of those nucleotide sequences can be calculated, for example, using the equation below [Bolton and McCarthy, 1962, (17):

10

15

20

$$T_m = 81.5^{\circ}\text{C} - 16.6(\log_{10}[\text{Na}^+]) + 0.41(\%G + C) - 0.63(\%\text{formamide}) - 600/l,$$

where  $l$  = the length of the hybrid in basepairs.

Stringent wash conditions include, for example, 4X SSC at 65°C, or 50% formamide, 4X SSC at 28°C, or 0.5X SSC, 0.1% SDS at 65°C. Highly stringent wash conditions include, for example, 0.2X SSC at 65°C.

25

The biological function of the identified genes may be more directly assessed by utilizing relevant in vivo and in vitro systems. In vivo systems may include, but are not limited to, animal systems which naturally exhibit breast cancer predisposition, or ones which have been engineered to exhibit such symptoms, including but not limited to oncogene overexpression (e.g. HER2/neu, ras, raf, or EGFR) malignant neoplasia mouse.

30

Splice variants derived from the same genomic region, encoded by the same pre mRNA can be identified by hybridization conditions described above for homology search. The specific characteristics of variant proteins encoded by splice variants of the same pre transcript may differ and can also be assayed as disclosed. A „BREAST  
5 CANCER GENE“ polynucleotide having a nucleotide sequence of one of the sequences of the SEQ ID NO: 1 to 165 or the complement thereof may therefor differ in parts of the entire sequence. The prediction of splicing events and the identification of the utilized acceptor and donor sites within the pre mRNA can be  
10 computed (e.g. Software Package GRAIL or GenomeSCAN) and verified by PCR method by those with skill in the art.

#### Antisense oligonucleotides

15 Antisense oligonucleotides are nucleotide sequences which are complementary to a specific DNA or RNA sequence. Once introduced into a cell, the complementary nucleotides combine with natural sequences produced by the cell to form complexes and block either transcription or translation. Preferably, an antisense oligonucleotide is at least 6 nucleotides in length, but can be at least 7, 8, 10, 12, 15, 20, 25, 30, 35,  
20 40, 45, or 50 or more nucleotides long. Longer sequences also can be used. Antisense oligonucleotide molecules can be provided in a DNA construct and introduced into a cell as described above to alter the level of „BREAST CANCER GENE“ gene products in the cell.

25 Antisense oligonucleotides can be deoxyribonucleotides, ribonucleotides, peptide nucleic acids (PNAs; described in U.S. Pat. No. 5,714,331), locked nucleic acids (LNAs; described in WO 99/12826), or a combination of them. Oligonucleotides can be synthesized manually or by an automated synthesizer, by covalently linking the 5' end of one nucleotide with the 3' end of another nucleotide with non-phosphodiester  
30 internucleotide linkages such alkylphosphonates, phosphorothioates, phosphorodithioates, alkylphosphonothioates, alkylphosphonates, phosphoramidates, phosphate



esters, carbamates, acetamidate, carboxymethyl esters, carbonates, and phosphate triesters[Brown, 1994, (55); Sonveaux, 1994, (56) and Uhlmann et al., 1990, (57)].

5 Modifications of „BREAST CANCER GENE“ expression can be obtained by designing antisense oligonucleotides which will form duplexes to the control, 5', or regulatory regions of the „BREAST CANCER GENE“. Oligonucleotides derived from the transcription initiation site, e.g., between positions 10 and +10 from the start site, are preferred. Similarly, inhibition can be achieved using "triple helix" base-pairing methodology. Triple helix pairing is useful because it causes inhibition of the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors, or chaperons. Therapeutic advances using triplex DNA have been described in the literature [Gee et al., 1994, (58)]. An antisense oligonucleotide also can be designed to block translation of mRNA by preventing the transcript from binding to ribosomes.

15 Precise complementarity is not required for successful complex formation between an antisense oligonucleotide and the complementary sequence of a „BREAST CANCER GENE“ polynucleotide. Antisense oligonucleotides which comprise, for example, 2, 3, 4, or 5 or more stretches of contiguous nucleotides which are precisely complementary to a „BREAST CANCER GENE“ polynucleotide, each separated by a stretch of contiguous nucleotides which are not complementary to adjacent „BREAST CANCER GENE“ nucleotides, can provide sufficient targeting specificity for „BREAST CANCER GENE“ mRNA. Preferably, each stretch of complementary contiguous nucleotides is at least 4, 5, 6, 7, or 8 or more nucleotides in length. Non-complementary intervening sequences are preferably 1, 2, 3, or 4 nucleotides in length. One skilled in the art can easily use the calculated melting point of an antisense-sense pair to determine the degree of mismatching which will be tolerated between a particular antisense oligonucleotide and a particular „BREAST CANCER GENE“ polynucleotide sequence.

Antisense oligonucleotides can be modified without affecting their ability to hybridize to a „BREAST CANCER GENE“ polynucleotide. These modifications can be internal or at one or both ends of the antisense molecule. For example, internucleoside phosphate linkages can be modified by adding cholesteryl or diamine  
5 moieties with varying numbers of carbon residues between the amino groups and terminal ribose. Modified bases and/or sugars, such as arabinose instead of ribose, or a 3', 5' substituted oligonucleotide in which the 3' hydroxyl group or the 5' phosphate group are substituted, also can be employed in a modified antisense oligonucleotide. These modified oligonucleotides can be prepared by methods well known in the art[  
10 Agrawal et al., 1992, (59); Uhlmann et al., 1987, (57) and Uhlmann et al., 2000 (60)].

### Ribozymes

Ribozymes are RNA molecules with catalytic activity [Cech, 1987, (61); Cech, 1990, (62) and Couture & Stinchcomb, 1996, (63)]. Ribozymes can be used to inhibit gene  
15 function by cleaving an RNA sequence, as is known in the art (e.g., Haseloff et al., U.S. Patent 5,641,673). The mechanism of ribozyme action involves sequence-specific hybridization of the ribozyme molecule to complementary target RNA, followed by endonucleolytic cleavage. Examples include engineered hammerhead  
20 motif ribozyme molecules that can specifically and efficiently catalyze endonucleolytic cleavage of specific nucleotide sequences.

The transcribed sequence of a „BREAST CANCER GENE“ can be used to generate ribozymes which will specifically bind to mRNA transcribed from a „BREAST  
25 CANCER GENE“ genomic locus. Methods of designing and constructing ribozymes which can cleave other RNA molecules in trans in a highly sequence specific manner have been developed and described in the art [Haseloff et al., 1988, (64)]. For example, the cleavage activity of ribozymes can be targeted to specific RNAs by engineering a discrete "hybridization" region into the ribozyme. The hybridization  
30 region contains a sequence complementary to the target RNA and thus specifically hybridizes with the target [see, for example, Gerlach et al., EP 0 321201].

Specific ribozyme cleavage sites within a „BREAST CANCER GENE“ RNA target can be identified by scanning the target molecule for ribozyme cleavage sites which include the following sequences: GUA, GUU, and GUC. Once identified, short RNA sequences of between 15 and 20 ribonucleotides corresponding to the region of the target RNA containing the cleavage site can be evaluated for secondary structural features which may render the target inoperable. Suitability of candidate „BREAST CANCER GENE“ RNA targets also can be evaluated by testing accessibility to hybridization with complementary oligonucleotides using ribonuclease protection assays. Longer complementary sequences can be used to increase the affinity of the hybridization sequence for the target. The hybridizing and cleavage regions of the ribozyme can be integrally related such that upon hybridizing to the target RNA through the complementary regions, the catalytic region of the ribozyme can cleave the target.

Ribozymes can be introduced into cells as part of a DNA construct. Mechanical methods, such as microinjection, liposome-mediated transfection, electroporation, or calcium phosphate precipitation, can be used to introduce a ribozyme-containing DNA construct into cells in which it is desired to decrease „BREAST CANCER GENE“ expression. Alternatively, if it is desired that the cells stably retain the DNA construct, the construct can be supplied on a plasmid and maintained as a separate element or integrated into the genome of the cells, as is known in the art. A ribozyme-encoding DNA construct can include transcriptional regulatory elements, such as a promoter element, an enhancer or UAS element, and a transcriptional terminator signal, for controlling transcription of ribozymes in the cells.

As taught in Haseloff et al., U.S Pat. No. 5,641,673, ribozymes can be engineered so that ribozyme expression will occur in response to factors which induce expression of a target gene. Ribozymes also can be engineered to provide an additional level of regulation, so that destruction of mRNA occurs only when both a ribozyme and a target gene are induced in the cells.

Polypeptides

“BREAST CANCER GENE” polypeptides according to the invention comprise an  
5 polypeptide selected from SEQ ID NO: 166 to 330 or encoded by any of the poly-  
nucleotide sequences of the SEQ ID NO: 1 to 165 or derivatives, fragments,  
analogues and homologues thereof. A “BREAST CANCER GENE” polypeptide of  
the invention therefore can be a portion, a full-length, or a fusion protein comprising  
all or a portion of a “BREAST CANCER GENE” polypeptide.

Protein Purification

„BREAST CANCER GENE“ polypeptides can be purified from any cell which  
expresses the responding protein, including host cells which have been transfected  
15 with „BREAST CANCER GENE“ expression constructs.. A purified „BREAST  
CANCER GENE“ polypeptide is separated from other compounds which are  
normally associate with the „BREAST CANCER GENE“ polypeptide in the cell,  
such as certain proteins, carbohydrates, or lipids, using methods well-known in the  
art. Such methods include, but are not limited to, size exclusion chromatography,  
20 ammonium sulfate fractionation, ion exchange chromatography, affinity chromato-  
graphy, and preparative gel electrophoresis. A preparation of purified „BREAST  
CANCER GENE“ polypeptides is at least 80% pure; preferably, the preparations are  
90%, 95%, or 99% pure. Purity of the preparations can be assessed by any means  
known in the art, such as SDS-polyacrylamide gel electrophoresis.

Obtaining Polypeptides

„BREAST CANCER GENE“ polypeptides can be obtained, for example, by purifi-  
cation from human cells, by expression of „BREAST CANCER GENE“ poly-  
30 nucleotides, or by direct chemical synthesis.

Biologically Active Variants

5 „BREAST CANCER GENE“ polypeptide variants which are biologically active, i.e., retain an „BREAST CANCER GENE“ activity, can be also regarded as „BREAST CANCER GENE“ polypeptides. Preferably, naturally or non-naturally occurring „BREAST CANCER GENE“ polypeptide variants have amino acid sequences which are at least about 60, 65, or 70, preferably about 75, 80, 85, 90, 92, 94, 96, or 98% identical to any of the amino acid sequences of the polypeptides of SEQ ID NO: 166 to 330 or the polypeptides encoded by any of the polynucleotides of SEQ ID NO: 1 to 165 or a fragment thereof. Percent identity between a putative „BREAST CANCER GENE“ polypeptide variant and of the polypeptides of SEQ ID NO: 166 to 330 polypeptides encoded by any of the polynucleotides of SEQ ID NO: 1 to 165 or a fragment thereof is determined by conventional methods. [See, for example, Altschul *et al.*, 1986, (19) and Henikoff & Henikoff, 1992, (20)]. Briefly, two amino acid sequences are aligned to optimize the alignment scores using a gap opening penalty of 10, a gap extension penalty of 1, and the “BLOSUM62” scoring matrix of Henikoff & Henikoff, 1992 (20).

20 Those skilled in the art appreciate that there are many established algorithms available to align two amino acid sequences. The “FASTA” similarity search algorithm of Pearson & Lipman is a suitable protein alignment method for examining the level of identity shared by an amino acid sequence disclosed herein and the amino acid sequence of a putative variant [Pearson & Lipman, 1988, (21), and Pearson, 1990, (22)]. Briefly, FASTA first characterizes sequence similarity by identifying regions shared by the query sequence (*e.g.*, SEQ ID NO: 1 to 165) and a test sequence that have either the highest density of identities (if the ktup variable is 1) or pairs of identities (if ktup=2), without considering conservative amino acid substitutions, insertions, or deletions. The ten regions with the highest density of identities are then rescored by comparing the similarity of all paired amino acids using an amino acid substitution matrix, and the ends of the regions are “trimmed” to include only those residues that contribute to the highest score. If there are several

regions with scores greater than the "cutoff" value (calculated by a predetermined formula based upon the length of the sequence the ktup value), then the trimmed initial regions are examined to determine whether the regions can be joined to form an approximate alignment with gaps. Finally, the highest scoring regions of the two amino acid sequences are aligned using a modification of the Needleman-Wunsch-Sellers algorithm [Needleman & Wunsch, 1970, (23), and Sellers, 1974, (24)], which allows for amino acid insertions and deletions. Preferred parameters for FASTA analysis are: ktup=1, gap opening penalty=10, gap extension penalty=1, and substitution matrix=BLOSUM62. These parameters can be introduced into a FASTA program by modifying the scoring matrix file ("SMATRIX"), as explained in Appendix 2 of Pearson, (22).

FASTA can also be used to determine the sequence identity of nucleic acid molecules using a ratio as disclosed above. For nucleotide sequence comparisons, the ktup value can range between one to six, preferably from three to six, most preferably three, with other parameters set as default.

Variations in percent identity can be due, for example, to amino acid substitutions, insertions, or deletions. Amino acid substitutions are defined as one for one amino acid replacements. They are conservative in nature when the substituted amino acid has similar structural and/or chemical properties. Examples of conservative replacements are substitution of a leucine with an isoleucine or valine, an aspartate with a glutamate, or a threonine with a serine.

Amino acid insertions or deletions are changes to or within an amino acid sequence. They typically fall in the range of about 1 to 5 amino acids. Guidance in determining which amino acid residues can be substituted, inserted, or deleted without abolishing biological or immunological activity of a „BREAST CANCER GENE“ polypeptide can be found using computer programs well known in the art, such as DNASTAR software. Whether an amino acid change results in a biologically active „BREAST CANCER GENE“ polypeptide can readily be determined by assaying for „BREAST

CANCER GENE" activity, as described for example, in the specific Examples, below. Larger insertions or deletions can also be caused by alternative splicing. Protein domains can be inserted or deleted without altering the main activity of the protein.

5

### Fusion Proteins

10 Fusion proteins are useful for generating antibodies against „BREAST CANCER GENE" polypeptide amino acid sequences and for use in various assay systems. For example, fusion proteins can be used to identify proteins which interact with portions of a „BREAST CANCER GENE" polypeptide. Protein affinity chromatography or library-based assays for protein-protein interactions, such as the yeast two-hybrid or phage display systems, can be used for this purpose. Such methods are well known in the art and also can be used as drug screens.

15

20 A „BREAST CANCER GENE" polypeptide fusion protein comprises two polypeptide segments fused together by means of a peptide bond. The first polypeptide segment comprises at least 25, 50, 75, 100, 150, 200, 300, 400, 500, 600, 700 or 750 contiguous amino acids of an amino acid sequence encoded by any polynucleotide sequences of the SEQ ID NO: 1 to 165 or of a biologically active variant, such as those described above. The first polypeptide segment also can comprise full-length „BREAST CANCER GENE".

25 The second polypeptide segment can be a full-length protein or a protein fragment. Proteins commonly used in fusion protein construction include  $\beta$ -galactosidase,  $\beta$ -glucuronidase, green fluorescent protein (GFP), autofluorescent proteins, including blue fluorescent protein (BFP), glutathione-S-transferase (GST), luciferase, horseradish peroxidase (HRP), and chloramphenicol acetyltransferase (CAT). Additionally, epitope tags are used in fusion protein constructions, including histidine (His) tags, FLAG tags, influenza hemagglutinin (HA) tags, Myc tags, VSV-G tags, and thioredoxin (Trx) tags. Other fusion constructions can include maltose binding

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protein (MBP), S- tag, Lex a DNA binding domain (DBD) fusions, GAL4 DNA binding domain fusions, and herpes simplex virus (HSV) BP16 protein fusions. A fusion protein also can be engineered to contain a cleavage site located between the „BREAST CANCER GENE“ polypeptide-encoding sequence and the heterologous protein sequence, so that the „BREAST CANCER GENE“ polypeptide can be cleaved and purified away from the heterologous moiety.

A fusion protein can be synthesized chemically, as is known in the art. Preferably, a fusion protein is produced by covalently linking two polypeptide segments or by standard procedures in the art of molecular biology. Recombinant DNA methods can be used to prepare fusion proteins, for example, by making a DNA construct which comprises coding sequences selected from any of the polynucleotide sequences of the SEQ ID NO: 1 to 165 in proper reading frame with nucleotides encoding the second polypeptide segment and expressing the DNA construct in a host cell, as is known in the art. Many kits for constructing fusion proteins are available from companies such as Promega Corporation (Madison, WI), Stratagene (La Jolla, CA), CLONTECH (Mountain View, CA), Santa Cruz Biotechnology (Santa Cruz, CA), MBL International Corporation (MIC; Watertown, MA), and Quantum Biotechnologies (Montreal, Canada; 1-888-DNA-KITS).

#### Identification of Species Homologues

Species homologues of human a „BREAST CANCER GENE“ polypeptide can be obtained using „BREAST CANCER GENE“ polynucleotides (described below) to make suitable probes or primers for screening cDNA expression libraries from other species, such as mice, monkeys, or yeast, identifying cDNAs which encode homologues of a „BREAST CANCER GENE“ polypeptide, and expressing the cDNAs as is known in the art.



Expression of Polynucleotides

To express a „BREAST CANCER GENE“ polynucleotide, the polynucleotide can be inserted into an expression vector which contains the necessary elements for the transcription and translation of the inserted coding sequence. Methods which are well known to those skilled in the art can be used to construct expression vectors containing sequences encoding „BREAST CANCER GENE“ polypeptides and appropriate transcriptional and translational control elements. These methods include in vitro recombinant DNA techniques, synthetic techniques, and in vivo genetic recombination. Such techniques are described, for example, in Sambrook et al., (6) and in Ausubel et al., (7).

A variety of expression vector/host systems can be utilized to contain and express sequences encoding a „BREAST CANCER GENE“ polypeptide. These include, but are not limited to, microorganisms, such as bacteria transformed with recombinant bacteriophage, plasmid, or cosmid DNA expression vectors; yeast transformed with yeast expression vectors, insect cell systems infected with virus expression vectors (e.g., baculovirus), plant cell systems transformed with virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or with bacterial expression vectors (e.g., Ti or pBR322 plasmids), or animal cell systems.

The control elements or regulatory sequences are those regions of the vector enhancers, promoters, 5' and 3' untranslated regions which interact with host cellular proteins to carry out transcription and translation. Such elements can vary in their strength and specificity. Depending on the vector system and host utilized, any number of suitable transcription and translation elements, including constitutive and inducible promoters, can be used. For example, when cloning in bacterial systems, inducible promoters such as the hybrid lacZ promoter of the BLUESCRIPT phagemid (Stratagene, LaJolla, Calif.) or pSPORT1 plasmid (Life Technologies) and the like can be used. The baculovirus polyhedrin promoter can be used in insect cells. Promoters or enhancers derived from the genomes of plant cells (e.g., heat shock,

RUBISCO, and storage protein genes) or from plant viruses (e.g., viral promoters or leader sequences) can be cloned into the vector. In mammalian cell systems, promoters from mammalian genes or from mammalian viruses are preferable. If it is necessary to generate a cell line that contains multiple copies of a nucleotide sequence encoding a „BREAST CANCER GENE“ polypeptide, vectors based on SV40 or EBV can be used with an appropriate selectable marker.

#### Bacterial and Yeast Expression Systems

In bacterial systems, a number of expression vectors can be selected depending upon the use intended for the „BREAST CANCER GENE“ polypeptide. For example, when a large quantity of the „BREAST CANCER GENE“ polypeptide is needed for the induction of antibodies, vectors which direct high level expression of fusion proteins that are readily purified can be used. Such vectors include, but are not limited to, multifunctional *E. coli* cloning and expression vectors such as BLUESCRIPT (Stratagene). In a BLUESCRIPT vector, a sequence encoding the „BREAST CANCER GENE“ polypeptide can be ligated into the vector in frame with sequences for the amino terminal Met and the subsequent 7 residues of  $\beta$ -galactosidase so that a hybrid protein is produced. pIN vectors [Van Heeke & Schuster, (113) ] or pGEX vectors (Promega, Madison, Wis.) also can be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption to glutathione agarose beads followed by elution in the presence of free glutathione. Proteins made in such systems can be designed to include heparin, thrombin, or factor Xa protease cleavage sites so that the cloned polypeptide of interest can be released from the GST moiety at will.

In the yeast *Saccharomyces cerevisiae*, a number of vectors containing constitutive or inducible promoters such as alpha factor, alcohol oxidase, and PGH can be used. For reviews, see Ausubel et al., (7) and Grant et al., (114).

### Plant and Insect Expression Systems

If plant expression vectors are used, the expression of sequences encoding „BREAST  
CANCER GENE“ polypeptides can be driven by any of a number of promoters. For  
5 example, viral promoters such as the 35S and 19S promoters of CaMV can be used  
alone or in combination with the omega leader sequence from TMV [Takamatsu,  
1987, (25)]. Alternatively, plant promoters such as the small subunit of RUBISCO or  
heat shock promoters can be used [Coruzzi et al., 1984, (26); Broglie et al., 1984,  
(27); Winter et al., 1991, (28)]. These constructs can be introduced into plant cells by  
10 direct DNA transformation or by pathogen-mediated transfection. Such techniques  
are described in a number of generally available reviews.

An insect system also can be used to express a „BREAST CANCER GENE“ poly-  
peptide. For example, in one such system *Autographa californica* nuclear poly-  
15 hedrosis virus (AcNPV) is used as a vector to express foreign genes in *Spodoptera*  
*frugiperda* cells or in *Trichoplusia* larvae. Sequences encoding „BREAST CANCER  
GENE“ polypeptides can be cloned into a nonessential region of the virus, such as  
the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful  
insertion of „BREAST CANCER GENE“ polypeptides will render the polyhedrin  
20 gene inactive and produce recombinant virus lacking coat protein. The recombinant  
viruses can then be used to infect *S. frugiperda* cells or *Trichoplusia* larvae in which  
„BREAST CANCER GENE“ polypeptides can be expressed [Engelhard et al., 1994,  
(29)].

### 25 Mammalian Expression Systems

A number of viral-based expression systems can be used to express „BREAST  
CANCER GENE“ polypeptides in mammalian host cells. For example, if an  
adenovirus is used as an expression vector, sequences encoding „BREAST CANCER  
30 GENE“ polypeptides can be ligated into an adenovirus transcription/translation  
complex comprising the late promoter and tripartite leader sequence. Insertion in a

nonessential E1 or E3 region of the viral genome can be used to obtain a viable virus which is capable of expressing a „BREAST CANCER GENE“ polypeptide in infected host cells [Logan & Shenk, 1984, (30)]. If desired, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, can be used to increase expression in mammalian host cells.

Human artificial chromosomes (HACs) also can be used to deliver larger fragments of DNA than can be contained and expressed in a plasmid. HACs of 6M to 10M are constructed and delivered to cells via conventional delivery methods (e.g., liposomes, polycationic amino polymers, or vesicles).

Specific initiation signals also can be used to achieve more efficient translation of sequences encoding „BREAST CANCER GENE“ polypeptides. Such signals include the ATG initiation codon and adjacent sequences. In cases where sequences encoding a „BREAST CANCER GENE“ polypeptide, its initiation codon, and upstream sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a fragment thereof, is inserted, exogenous translational control signals (including the ATG initiation codon) should be provided. The initiation codon should be in the correct reading frame to ensure translation of the entire insert. Exogenous translational elements and initiation codons can be of various origins both natural and synthetic. The efficiency of expression can be enhanced by the inclusion of enhancers which are appropriate for the particular cell system which is used [Scharf et al., 1994, (31)].

### Host Cells

A host cell strain can be chosen for its ability to modulate the expression of the inserted sequences or to process the expressed „BREAST CANCER GENE“ polypeptide in the desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation,

lipidation, and acylation. Posttranslational processing which cleaves a "prepro" form of the polypeptide also can be used to facilitate correct insertion, folding and/or function. Different host cells which have specific cellular machinery and characteristic mechanisms for Post-translational activities (e.g., CHO, HeLa, MDCK, HEK293, and WI38), are available from the American Type Culture Collection (ATCC; 10801 University Boulevard, Manassas, VA 20110-2209) and can be chosen to ensure the correct modification and processing of the foreign protein.

Stable expression is preferred for long-term, high-yield production of recombinant proteins. For example, cell lines which stably express „BREAST CANCER GENE“ polypeptides can be transformed using expression vectors which can contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells can be allowed to grow for 12 days in an enriched medium before they are switched to a selective medium. The purpose of the selectable marker is to confer resistance to selection, and its presence allows growth and recovery of cells which successfully express the introduced „BREAST CANCER GENE“ sequences. Resistant clones of stably transformed cells can be proliferated using tissue culture techniques appropriate to the cell type [Freshney et al., 1986, (32)].

Any number of selection systems can be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase (Wigler et al., 1977, (33)) and adenine phosphoribosyltransferase [Lowy et al., 1980, (34)] genes which can be employed in  $tk^-$  or  $aprt^-$  cells, respectively. Also, antimetabolite, antibiotic, or herbicide resistance can be used as the basis for selection. For example,  $dhfr$  confers resistance to methotrexate [Wigler et al., 1980, (35)],  $npt$  confers resistance to the aminoglycosides, neomycin and G418 [Colbere-Garapin et al., 1981, (36)], and  $als$  and  $pat$  confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively. Additional selectable genes have been described. For example,  $trpB$  allows cells to utilize indole in place of tryptophan, or  $hisD$ , which allows cells to utilize histinol in place of histidine

[Hartman & Mulligan, 1988 ,(37)]. Visible markers such as anthocyanins,  $\beta$ -glucuronidase and its substrate GUS, and luciferase and its substrate luciferin, can be used to identify transformants and to quantify the amount of transient or stable protein expression attributable to a specific vector system [Rhodes et al., 1995, (38)].

5

Detecting Expression and gene product

Although the presence of marker gene expression suggests that the „BREAST  
CANCER GENE“ polynucleotide is also present, its presence and expression may  
10 need to be confirmed. For example, if a sequence encoding a „BREAST CANCER  
GENE“ polypeptide is inserted within a marker gene sequence, transformed cells  
containing sequences which encode a „BREAST CANCER GENE“ polypeptide can  
be identified by the absence of marker gene function. Alternatively, a marker gene  
can be placed in tandem with a sequence encoding a „BREAST CANCER GENE“  
15 polypeptide under the control of a single promoter. Expression of the marker gene in  
response to induction or selection usually indicates expression of the „BREAST  
CANCER GENE“ polynucleotide.

Alternatively, host cells which contain a „BREAST CANCER GENE“ poly-  
20 nucleotide and which express a „BREAST CANCER GENE“ polypeptide can be  
identified by a variety of procedures known to those of skill in the art. These  
procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridization  
and protein bioassay or immunoassay techniques which include membrane, solution,  
or chip-based technologies for the detection and/or quantification of polynucleotide  
25 or protein. For example, the presence of a polynucleotide sequence encoding a  
„BREAST CANCER GENE“ polypeptide can be detected by DNA-DNA or DNA-  
RNA hybridization or amplification using probes or fragments or fragments of  
polynucleotides encoding a „BREAST CANCER GENE“ polypeptide. Nucleic acid  
amplification-based assays involve the use of oligonucleotides selected from  
30 sequences encoding a „BREAST CANCER GENE“ polypeptide to detect  
transformants which contain a „BREAST CANCER GENE“ polynucleotide.

5 A variety of protocols for detecting and measuring the expression of a „BREAST  
CANCER GENE“ polypeptide, using either polyclonal or monoclonal antibodies  
specific for the polypeptide, are known in the art. Examples include enzyme-linked  
immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescence activated  
cell sorting (FACS). A two-site, monoclonal-based immunoassay using monoclonal  
antibodies reactive to two non-interfering epitopes on a „BREAST CANCER  
GENE“ polypeptide can be used, or a competitive binding assay can be employed.  
These and other assays are described in Hampton et al., (39) and Maddox et al., 40).

10 A wide variety of labels and conjugation techniques are known by those skilled in the  
art and can be used in various nucleic acid and amino acid assays. Means for  
producing labeled hybridization or PCR probes for detecting sequences related to  
polynucleotides encoding „BREAST CANCER GENE“ polypeptides include oligo  
15 labeling, nick translation, end-labeling, or PCR amplification using a labeled  
nucleotide. Alternatively, sequences encoding a „BREAST CANCER GENE“ poly-  
peptide can be cloned into a vector for the production of an mRNA probe. Such  
vectors are known in the art, are commercially available, and can be used to  
synthesize RNA probes in vitro by addition of labeled nucleotides and an appropriate  
20 RNA polymerase such as T7, T3, or SP6. These procedures can be conducted using a  
variety of commercially available kits (Amersham Pharmacia Biotech, Promega, and  
US Biochemical). Suitable reporter molecules or labels which can be used for ease of  
detection include radionuclides, enzymes, and fluorescent, chemiluminescent, or  
chromogenic agents, as well as substrates, cofactors, inhibitors, magnetic particles,  
25 and the like.

#### Expression and Purification of Polypeptides

30 Host cells transformed with nucleotide sequences encoding a „BREAST CANCER  
GENE“ polypeptide can be cultured under conditions suitable for the expression and  
recovery of the protein from cell culture. The polypeptide produced by a transformed

cell can be secreted or stored intracellular depending on the sequence and/or the vector used. As will be understood by those of skill in the art, expression vectors containing polynucleotides which encode „BREAST CANCER GENE“ polypeptides can be designed to contain signal sequences which direct secretion of soluble  
5 „BREAST CANCER GENE“ polypeptides through a prokaryotic or eukaryotic cell membrane or which direct the membrane insertion of membrane-bound „BREAST CANCER GENE“ polypeptide.

As discussed above, other constructions can be used to join a sequence encoding a  
10 „BREAST CANCER GENE“ polypeptide to a nucleotide sequence encoding a polypeptide domain which will facilitate purification of soluble proteins. Such purification facilitating domains include, but are not limited to, metal chelating peptides such as histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized immunoglobulin,  
15 and the domain utilized in the FLAGS extension/affinity purification system (Immunex Corp., Seattle, Wash.). Inclusion of cleavable linker sequences such as those specific for Factor Xa or enterokinase (Invitrogen, San Diego, CA) between the purification domain and the „BREAST CANCER GENE“ polypeptide also can be used to facilitate purification. One such expression vector provides for expression of  
20 a fusion protein containing a „BREAST CANCER GENE“ polypeptide and 6 histidine residues preceding a thioredoxin or an enterokinase cleavage site. The histidine residues facilitate purification by IMAC (immobilized metal ion affinity chromatography [Porath et al., 1992, (41)], while the enterokinase cleavage site provides a means for purifying the „BREAST CANCER GENE“ polypeptide from  
25 the fusion protein. Vectors which contain fusion proteins are disclosed in Kroll et al., (42).

### Chemical Synthesis

30 Sequences encoding a „BREAST CANCER GENE“ polypeptide can be synthesized, in whole or in part, using chemical methods well known in the art (see Caruthers et



al., (43) and Horn et al., (44). Alternatively, a „BREAST CANCER GENE“ polypeptide itself can be produced using chemical methods to synthesize its amino acid sequence, such as by direct peptide synthesis using solid-phase techniques [Merrifield, 1963, (45) and Roberge et al., 1995, (46)]. Protein synthesis can be performed using manual techniques or by automation. Automated synthesis can be achieved, for example, using Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer). Optionally, fragments of „BREAST CANCER GENE“ polypeptides can be separately synthesized and combined using chemical methods to produce a full-length molecule.

The newly synthesized peptide can be substantially purified by preparative high performance liquid chromatography [Creighton, 1983, (47)]. The composition of a synthetic „BREAST CANCER GENE“ polypeptide can be confirmed by amino acid analysis or sequencing (e.g., the Edman degradation procedure; see Creighton, (47). Additionally, any portion of the amino acid sequence of the „BREAST CANCER GENE“ polypeptide can be altered during direct synthesis and/or combined using chemical methods with sequences from other proteins to produce a variant polypeptide or a fusion protein.

#### Production of Altered Polypeptides

As will be understood by those of skill in the art, it may be advantageous to produce „BREAST CANCER GENE“ polypeptide-encoding nucleotide sequences possessing non-natural occurring codons. For example, codons preferred by a particular prokaryotic or eukaryotic host can be selected to increase the rate of protein expression or to produce an RNA transcript having desirable properties, such as a half-life which is longer than that of a transcript generated from the naturally occurring sequence.

The nucleotide sequences disclosed herein can be engineered using methods generally known in the art to alter „BREAST CANCER GENE“ polypeptide-

encoding sequences for a variety of reasons, including but not limited to, alterations which modify the cloning, processing, and/or expression of the polypeptide or mRNA product. DNA shuffling by random fragmentation and PCR re-assembly of gene fragments and synthetic oligonucleotides can be used to engineer the nucleotide sequences. For example, site-directed mutagenesis can be used to insert new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, introduce mutations, and so forth.

*Predictive, Diagnostic and Prognostic Assays*

10

The present invention provides compositions, methods, and kits for determining whether a subject is at risk for developing malignant neoplasia and breast cancer in particular by detecting the disclosed biomarkers, i.e., the disclosed polynucleotide markers comprising any of the polynucleotides sequences of the SEQ ID NO 1 to 165 and/or the polypeptide markers encoded thereby or polypeptide markers comprising any of the polypeptide sequences of the SEQ ID NO: 166 to 330 for malignant neoplasia and breast cancer in particular.

20

In clinical applications, biological samples can be screened for the presence and/or absence of the biomarkers identified herein. Such samples are for example needle biopsy cores, surgical resection samples, or body fluids like serum, thin needle nipple aspirates and urine. For example, these methods include obtaining a biopsy, which is optionally fractionated by cryostat sectioning to enrich diseased cells to about 80% of the total cell population. In certain embodiments, polynucleotides extracted from these samples may be amplified using techniques well known in the art. The expression levels of selected markers detected would be compared with statistically valid groups of diseased and healthy samples.

30

In one embodiment the compositions, methods, and kits comprises determining whether a subject has an abnormal mRNA and/or protein level of the disclosed markers, such as by Northern blot analysis, reverse transcription-polymerase chain

reaction (RT-PCR), in situ hybridization, immunoprecipitation, Western blot hybridization, or immunohistochemistry. According to the method, cells are obtained from a subject and the levels of the disclosed biomarkers, protein or mRNA level, is determined and compared to the level of these markers in a healthy subject. An  
5 abnormal level of the biomarker polypeptide or mRNA levels is likely to be indicative of malignant neoplasia such as breast cancer.

In another embodiment the compositions, methods, and kits comprises determining whether a subject has an abnormal DNA content of said genes or said genomic loci,  
10 such as by Southern blot analysis, dot blot analysis, Fluorescence or Colorimetric In Situ Hybridization, Comparative Genomic Hybridization or quantitative PCR. In general these assays comprise the usage of probes from representative genomic regions. The probes contain at least parts of said genomic regions or sequences  
15 complementary or analogous to said regions. In particular intra- or intergenic regions of said genes or genomic regions. The probes can consist of nucleotide sequences or sequences of analogous functions (e.g. PNAs, Morpholino oligomers) being able to bind to target regions by hybridization. In general genomic regions being altered in  
20 said patient samples are compared with unaffected control samples (normal tissue from the same or different patients, surrounding unaffected tissue, peripheral blood) or with genomic regions of the same sample that don't have said alterations and can therefore serve as internal controls. In a preferred embodiment regions located on the  
25 same chromosome are used. Alternatively, gonosomal regions and /or regions with defined varying amount in the sample are used. In one favored embodiment the DNA content, structure, composition or modification is compared that lie within distinct  
30 genomic regions. Especially favored are methods that detect the DNA content of said samples, where the amount of target regions are altered by amplification and or deletions. In another embodiment the target regions are analyzed for the presence of polymorphisms (e.g. Single Nucleotide Polymorphisms or mutations) that affect or predispose the cells in said samples with regard to clinical aspects, being of diagnostic, prognostic or therapeutic value. Preferably, the identification of sequence

variations is used to define haplotypes that result in characteristic behavior of said samples with said clinical aspects.

5 In one embodiment, the compositions, methods, and kits for the prediction, diagnosis or prognosis of malignant neoplasia and breast cancer in particular are done by the detection of:

- (a) a polynucleotide selected from the polynucleotides of the SEQ ID NO: 1 to 165;
- 10 (b) a polynucleotide which hybridizes under stringent conditions to a polynucleotide specified in (a) encoding a polypeptide exhibiting the same biological function as specified for the respective sequence in Table 1 or 4;
- 15 (c) a polynucleotide the sequence of which deviates from the polynucleotide specified in (a) and (b) due to the generation of the genetic code encoding a polypeptide exhibiting the same biological function as specified for the polypeptides of SEQ ID NO: 166 to 330
- 20 (d) a polynucleotide which represents a specific fragment, derivative or allelic variation of a polynucleotide sequence specified in (a) to (c) encoding a polypeptide exhibiting the same biological function as specified for the respective sequence in Table 1 or 4;

25 in a biological sample comprising the following steps: hybridizing any polynucleotide or analogous oligomer specified in (a) to (d) to a polynucleotide material of a biological sample, thereby forming a hybridization complex; and detecting said hybridization complex.

30 In another embodiment the method for the prediction, diagnosis or prognosis of malignant neoplasia is done as just described but, wherein before hybridization, the polynucleotide material of the biological sample is amplified.

In another embodiment the method for the diagnosis or prognosis of malignant neoplasia and breast cancer in particular is done by the detection of:

- 5 (a) a polynucleotide selected from the polynucleotides of the SEQ ID NO: 166 to 330;
- (b) a polynucleotide which hybridizes under stringent conditions to a polynucleotide specified in (a) encoding a polypeptide exhibiting the same biological function as specified for the respective sequence in Table 1 or 4;
- 10 (c) a polynucleotide the sequence of which deviates from the polynucleotide specified in (a) and (b) due to the generation of the genetic code encoding a polypeptide exhibiting the same biological function as specified for the respective sequence in Table 1 or 4;
- 15 (d) a polynucleotide which represents a specific fragment, derivative or allelic variation of a polynucleotide sequence specified in (a) to (c) encoding a polypeptide exhibiting the same biological function as specified for the respective sequence in Table 1 or 4;
- 20 (e) a polypeptide encoded by a polynucleotide sequence specified in (a) to (d)
- (f) a polypeptide comprising any polypeptide of SEQ ID NO: 166 to 330
- 25 (g) comprising the steps of contacting a biological sample with a reagent which specifically interacts with the polynucleotide specified in (a) to (d) or the polypeptide specified in (e).

1. DNA array technology

5 In one embodiment, the present Invention also provides a method wherein polynucleotide probes are immobilized on a DNA chip in an organized array. Oligonucleotides can be bound to a solid Support by a variety of processes, including lithography. For example a chip can hold up to 410,000 oligonucleotides (GeneChip, Affymetrix). The present invention provides significant advantages over the available tests for malignant neoplasia, such as breast cancer, because it increases the  
10 reliability of the test by providing an array of polynucleotide markers on a single chip.

The method includes obtaining a biological sample which can be a biopsy of an affected person, which is optionally fractionated by cryostat sectioning to enrich  
15 diseased cells to about 80% of the total cell population and the use of body fluids such as serum or urine, serum or cell containing liquids (e.g. derived from fine needle aspirates). The DNA or RNA is then extracted, amplified, and analyzed with a DNA chip to determine the presence or absence of the marker polynucleotide sequences. In one embodiment, the polynucleotide probes are spotted onto a substrate in a  
20 two-dimensional matrix or array. Samples of polynucleotides can be labeled and then hybridized to the probes. Double-stranded polynucleotides, comprising the labeled sample polynucleotides bound to probe polynucleotides, can be detected once the unbound portion of the sample is washed away.

25 The probe polynucleotides can be spotted on substrates including glass, nitrocellulose, etc. The probes can be bound to the substrate by either covalent bonds or by non-specific interactions, such as hydrophobic interactions. The sample polynucleotides can be labeled using radioactive labels, fluorophores, chromophores, etc. Techniques for constructing arrays and methods of using these arrays are  
30 described in EP 0 799 897; WO 97/29212; WO 97/27317; EP 0 785 280; WO 97/02357; U.S. Pat. No. 5,593,839; U.S. Pat. No. 5,578,832; EP 0 728 520; U.S. Pat.

No. 5,599,695; EP 0 721 016; U.S. Pat. No. 5,556,752; WO 95/22058; and U.S. Pat. No. 5,631,734. Further, arrays can be used to examine differential expression of genes and can be used to determine gene function. For example, arrays of the instant polynucleotide sequences can be used to determine if any of the polynucleotide sequences are differentially expressed between normal cells and diseased cells, for example. High expression of a particular message in a diseased sample, which is not observed in a corresponding normal sample, can indicate a breast cancer specific protein.

10 Accordingly, in one aspect, the invention provides probes and primers that are specific to the polynucleotide sequences of SEQ ID NO: 1 to 165.

15 In one embodiment, the composition, method, and kit comprise using a polynucleotide probe to determine the presence of malignant or breast cancer cells in particular in a tissue from a patient. Specifically, the method comprises:

- 1) providing a polynucleotide probe comprising a nucleotide sequence at least 12 nucleotides in length, preferably at least 15 nucleotides, more preferably, 25 nucleotides, and most preferably at least 40 nucleotides, and up to all or nearly all of the coding sequence which is complementary to a portion of the coding sequence of a polynucleotide selected from the polynucleotides of SEQ ID NO: 1 to 165 or a sequence complementary thereto;
- 2) obtaining a tissue sample from a patient with malignant neoplasia;
- 3) providing a second tissue sample from a patient with no malignant neoplasia;
- 4) contacting the polynucleotide probe under stringent conditions with RNA of each of said first and second tissue samples (e.g., in a Northern blot or in situ hybridization assay); and

5) comparing (a) the amount of hybridization of the probe with RNA of the first tissue sample, with (b) the amount of hybridization of the probe with RNA of the second tissue sample;

5 wherein a statistically significant difference in the amount of hybridization with the RNA of the first tissue sample as compared to the amount of hybridization with the RNA of the second tissue sample is indicative of malignant neoplasia and breast cancer in particular in the first tissue sample.

10 2. Data analysis methods

Comparison of the expression levels of one or more "BREAST CANCER GENES" with reference expression levels, e.g., expression levels in diseased cells of breast cancer or in normal counterpart cells, is preferably conducted using computer systems. In one embodiment, expression levels are obtained in two cells and these two sets of expression levels are introduced into a computer system for comparison. In a preferred embodiment, one set of expression levels is entered into a computer system for comparison with values that are already present in the computer system, or in computer-readable form that is then entered into the computer system.

20 In one embodiment, the invention provides a computer readable form of the gene expression profile data of the invention, or of values corresponding to the level of expression of at least one "BREAST CANCER GENE" in a diseased cell. The values can be mRNA expression levels obtained from experiments, e.g., microarray analysis. The values can also be mRNA levels normalised relative to a reference gene whose expression is constant in numerous cells under numerous conditions, e.g., GAPDH. In other embodiments, the values in the computer are ratios of, or differences between, normalized or non-normalized mRNA levels in different samples.

30



The gene expression profile data can be in the form of a table, such as an Excel table. The data can be alone, or it can be part of a larger database, e.g., comprising other expression profiles. For example, the expression profile data of the invention can be part of a public database. The computer readable form can be in a computer. In  
5 another embodiment, the invention provides a computer displaying the gene expression profile data.

In one embodiment, the invention provides a method for determining the similarity  
10 between the level of expression of one or more "BREAST CANCER GENES" in a first cell, e.g., a cell of a subject, and that in a second cell, comprising obtaining the level of expression of one or more "BREAST CANCER GENES" in a first cell and entering these values into a computer comprising a database including records comprising values corresponding to levels of expression of one or more "BREAST  
15 CANCER GENES" in a second cell, and processor instructions, e.g., a user interface, capable of receiving a selection of one or more values for comparison purposes with data that is stored in the computer. The computer may further comprise a means for converting the comparison data into a diagram or chart or other type of output.

In another embodiment, values representing expression levels of "BREAST  
20 CANCER GENES" are entered into a computer system, comprising one or more databases with reference expression levels obtained from more than one cell. For example, the computer comprises expression data of diseased and normal cells. Instructions are provided to the computer, and the computer is capable of comparing the data entered with the data in the computer to determine whether the data entered  
25 is more similar to that of a normal cell or of a diseased cell.

In another embodiment, the computer comprises values of expression levels in cells of subjects at different stages of breast cancer, and the computer is capable of comparing expression data entered into the computer with the data stored, and  
30 produce results indicating to which of the expression profiles in the computer, the

one entered is most similar, such as to determine the stage of breast cancer in the subject.

5 In yet another embodiment, the reference expression profiles in the computer are expression profiles from cells of breast cancer of one or more subjects, which cells are treated *in vivo* or *in vitro* with a drug used for therapy of breast cancer. Upon entering of expression data of a cell of a subject treated *in vitro* or *in vivo* with the drug, the computer is instructed to compare the data entered to the data in the computer, and to provide results indicating whether the expression data input into the  
10 computer are more similar to those of a cell of a subject that is responsive to the drug or more similar to those of a cell of a subject that is not responsive to the drug. Thus, the results indicate whether the subject is likely to respond to the treatment with the drug or unlikely to respond to it.

15 In one embodiment, the invention provides a system that comprises a means for receiving gene expression data for one or a plurality of genes; a means for comparing the gene expression data from each of said one or plurality of genes to a common reference frame; and a means for presenting the results of the comparison. This system may further comprise a means for clustering the data.

20 In another embodiment, the invention provides a computer program for analyzing gene expression data comprising (i) a computer code that receives as input gene expression data for a plurality of genes and (ii) a computer code that compares said gene expression data from each of said plurality of genes to a common reference  
25 frame.

The invention also provides a machine-readable or computer-readable medium including program instructions for performing the following steps: (i) comparing a plurality of values corresponding to expression levels of one or more genes  
30 characteristic of breast cancer in a query cell with a database including records comprising reference expression or expression profile data of one or more reference

cells and an annotation of the type of cell; and (ii) indicating to which cell the query cell is most similar based on similarities of expression profiles. The reference cells can be cells from subjects at different stages of breast cancer. The reference cells can also be cells from subjects responding or not responding to a particular drug treatment and optionally incubated *in vitro* or *in vivo* with the drug.

The reference cells may also be cells from subjects responding or not responding to several different treatments, and the computer system indicates a preferred treatment for the subject. Accordingly, the invention provides a method for selecting a therapy for a patient having breast cancer, the method comprising: (i) providing the level of expression of one or more genes characteristic of breast cancer in a diseased cell of the patient; (ii) providing a plurality of reference profiles, each associated with a therapy, wherein the subject expression profile and each reference profile has a plurality of values, each value representing the level of expression of a gene characteristic of breast cancer; and (iii) selecting the reference profile most similar to the subject expression profile, to thereby select a therapy for said patient. In a preferred embodiment step (iii) is performed by a computer. The most similar reference profile may be selected by weighing a comparison value of the plurality using a weight value associated with the corresponding expression data.

The relative abundance of an mRNA in two biological samples can be scored as a perturbation and its magnitude determined (i.e., the abundance is different in the two sources of mRNA tested), or as not perturbed (i.e., the relative abundance is the same). In various embodiments, a difference between the two sources of RNA of at least a factor of about 25% (RNA from one source is 25% more abundant in one source than the other source), more usually about 50%, even more often by a factor of about 2 (twice as abundant), 3 (three times as abundant) or 5 (five times as abundant) is scored as a perturbation. Perturbations can be used by a computer for calculating and expression comparisons.

Preferably, in addition to identifying a perturbation as positive or negative, it is advantageous to determine the magnitude of the perturbation. This can be carried out, as noted above, by calculating the ratio of the emission of the two fluorophores used for differential labeling, or by analogous methods that will be readily apparent to those of skill in the art.

The computer readable medium may further comprise a pointer to a descriptor of a stage of breast cancer or to a treatment for breast cancer.

In operation, the means for receiving gene expression data, the means for comparing the gene expression data, the means for presenting, the means for normalizing, and the means for clustering within the context of the systems of the present invention can involve a programmed computer with the respective functionalities described herein, implemented in hardware or hardware and software; a logic circuit or other component of a programmed computer that performs the operations specifically identified herein, dictated by a computer program; or a computer memory encoded with executable instructions representing a computer program that can cause a computer to function in the particular fashion described herein.

Those skilled in the art will understand that the systems and methods of the present invention may be applied to a variety of systems, including IBM-compatible personal computers running MS-DOS or Microsoft Windows.

The computer may have internal components linked to external components. The internal components may include a processor element interconnected with a main memory. The computer system can be an Intel Pentium<sup>®</sup>-based processor of 200 MHz or greater clock rate and with 32 MB or more of main memory. The external component may comprise a mass storage, which can be one or more hard disks (which are typically packaged together with the processor and memory). Such hard disks are typically of 1 GB or greater storage capacity. Other external components include a user interface device, which can be a monitor, together with an inputting

device, which can be a "mouse", or other graphic input devices, and/or a keyboard. A printing device can also be attached to the computer.

5 Typically, the computer system is also linked to a network link, which can be part of an Ethernet link to other local computer systems, remote computer systems, or wide area communication networks, such as the Internet. This network link allows the computer system to share data and processing tasks with other computer systems.

10 Loaded into memory during operation of this system are several software components, which are both standard in the art and special to the instant invention. These software components collectively cause the computer system to function according to the methods of this invention. These software components are typically stored on a mass storage. A software component represents the operating system, which is responsible for managing the computer system and its network interconnections. This  
15 operating system can be, for example, of the Microsoft Windows' family, such as Windows 95, Windows 98, or Windows NT. A software component represents common languages and functions conveniently present on this system to assist programs implementing the methods specific to this invention. Many high or low level computer languages can be used to program the analytic methods of this  
20 invention. Instructions can be interpreted during run-time or compiled. Preferred languages include C/C++, and JAVA®. Most preferably, the methods of this invention are programmed in mathematical software packages which allow symbolic entry of equations and high-level specification of processing, including algorithms to be used, thereby freeing a user of the need to procedurally program individual equations or algorithms. Such packages include Matlab from Mathworks (Natick, Mass.), Mathematica from Wolfram Research (Champaign, Ill.), or S-Plus from Math  
25 Soft (Cambridge, Mass.). Accordingly, a software component represents the analytic methods of this invention as programmed in a procedural language or symbolic package. In a preferred embodiment, the computer system also contains a database comprising values representing levels of expression of one or more genes  
30

characteristic of breast cancer. The database may contain one or more expression profiles of genes characteristic of breast cancer in different cells.

5 In an exemplary implementation, to practice the methods of the present invention, a user first loads expression profile data into the computer system. These data can be directly entered by the user from a monitor and keyboard, or from other computer systems linked by a network connection, or on removable storage media such as a CD-ROM or floppy disk or through the network. Next the user causes execution of expression profile analysis software which performs the steps of comparing and, e.g.,  
10 clustering co-varying genes into groups of genes.

In another exemplary implementation, expression profiles are compared using a method described in U.S. Patent No. 6,203,987. A user first loads expression profile data into the computer system. Geneset profile definitions are loaded into the  
15 memory from the storage media or from a remote computer, preferably from a dynamic geneset database system, through the network. Next the user causes execution of projection software which performs the steps of converting expression profile to projected expression profiles. The projected expression profiles are then displayed.

20 In yet another exemplary implementation, a user first leads a projected profile into the memory. The user then causes the loading of a reference profile into the memory. Next, the user causes the execution of comparison software which performs the steps of objectively comparing the profiles.

25

### 3. Detection of variant polynucleotide sequence

In yet another embodiment, the invention provides methods for determining whether a subject is at risk for developing a disease, such as a predisposition to develop  
30 malignant neoplasia, for example breast cancer, associated with an aberrant activity of any one of the polypeptides encoded by any of the polynucleotides of the SEQ ID

NO: 1 to 165, wherein the aberrant activity of the polypeptide is characterized by detecting the presence or absence of a genetic lesion characterized by at least one of these:

- 5       (i)     an alteration affecting the integrity of a gene encoding a marker polypeptides,  
          or  
       (ii)    the misexpression of the encoding polynucleotide.

10       To illustrate, such genetic lesions can be detected by ascertaining the existence of at least one of these:

- I.     a deletion of one or more nucleotides from the polynucleotide sequence
- 15       II.    an addition of one or more nucleotides to the polynucleotide sequence
- III.   a substitution of one or more nucleotides of the polynucleotide sequence
- IV.   a gross chromosomal rearrangement of the polynucleotide sequence
- 20       V.     a gross alteration in the level of a messenger RNA transcript of the polynucleotide sequence
- VI.   aberrant modification of the polynucleotide sequence, such as of the methylation pattern of the genomic DNA
- 25       VII.   the presence of a non-wild type splicing pattern of a messenger RNA transcript of the gene
- VIII.  a non-wild type level of the marker polypeptide
- 30       IX.    allelic loss of the gene

X. inappropriate post-translational modification of the marker polypeptide

5 The present invention provides assay techniques for detecting mutations in the encoding polynucleotide sequence. These methods include, but are not limited to, methods involving sequence analysis, Southern blot hybridization, restriction enzyme site mapping, and methods involving detection of absence of nucleotide pairing between the polynucleotide to be analyzed and a probe.

10 Specific diseases or disorders, e.g., genetic diseases or disorders, are associated with specific allelic variants of polymorphic regions of certain genes, which do not necessarily encode a mutated protein. Thus, the presence of a specific allelic variant of a polymorphic region of a gene in a subject can render the subject susceptible to developing a specific disease or disorder. Polymorphic regions in genes, can be  
15 identified, by determining the nucleotide sequence of genes in populations of individuals. If a polymorphic region is identified, then the link with a specific disease can be determined by studying specific populations of individuals, e.g. individuals which developed a specific disease, such as breast cancer. A polymorphic region can be located in any region of a gene, e.g., exons, in coding or non coding regions of  
20 exons, introns, and promoter region.

In an exemplary embodiment, there is provided a polynucleotide composition comprising a polynucleotide probe including a region of nucleotide sequence which is capable of hybridising to a sense or antisense sequence of a gene or naturally  
25 occurring mutants thereof, or 5' or 3' flanking sequences or intronic sequences naturally associated with the subject genes or naturally occurring mutants thereof. The polynucleotide of a cell is rendered accessible for hybridization, the probe is contacted with the polynucleotide of the sample, and the hybridization of the probe to the sample polynucleotide is detected. Such techniques can be used to detect lesions  
30 or allelic variants at either the genomic or mRNA level, including deletions, substitutions, etc., as well as to determine mRNA transcript levels.



5 A preferred detection method is allele specific hybridization using probes over-  
lapping the mutation or polymorphic site and having about 5, 10, 20, 25, or 30  
nucleotides around the mutation or polymorphic region. In a preferred embodiment  
of the invention, several probes capable of hybridising specifically to allelic variants  
are attached to a solid phase support, e.g., a "chip". Mutation detection analysis using  
these chips comprising oligonucleotides, also termed "DNA probe arrays" is  
described e.g., in Cronin et al. (48). In one embodiment, a chip comprises all the  
allelic variants of at least one polymorphic region of a gene. The solid phase support  
10 is then contacted with a test polynucleotide and hybridization to the specific probes is  
detected. Accordingly, the identity of numerous allelic variants of one or more genes  
can be identified in a simple hybridization experiment.

15 In certain embodiments, detection of the lesion comprises utilizing the probe/primer  
in a polymerase chain reaction (PCR) (see, e.g. U.S. Patent Nos. 4,683,195 and  
4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligase chain  
reaction (LCR) [Landegran et al., 1988, (49) and Nakazawa et al., 1994 (50)], the  
latter of which can be particularly useful for detecting point mutations in the gene;  
Abravaya et al., 1995 ,(51)]. In a merely illustrative embodiment, the method  
20 includes the steps of (i) collecting a sample of cells from a patient, (ii) isolating  
polynucleotide (e.g., genomic, mRNA or both) from the cells of the sample, (iii)  
contacting the polynucleotide sample with one or more primers which specifically  
hybridize to a polynucleotide sequence under conditions such that hybridization and  
amplification of the polynucleotide (if present) occurs, and (iv) detecting the  
25 presence or absence of an amplification product, or detecting the size of the  
amplification product and comparing the length to a control sample. It is anticipated  
that PCR and/or LCR may be desirable to use as a preliminary amplification step in  
conjunction with any of the techniques used for detecting mutations described herein.

30 Alternative amplification methods include: self sustained sequence replication  
[Guatelli, J.C. et al., 1990, (52)]; transcriptional amplification system [Kwoh, D.Y. et

al., 1989, (53)], Q-Beta replicase [Lizardi, P.M. et al., 1988 ,(54)], or any other polynucleotide amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection schemes are especially useful for the detection of polynucleotide molecules if such  
5 molecules are present in very low numbers.

In a preferred embodiment of the subject assay, mutations in, or allelic variants, of a gene from a sample cell are identified by alterations in restriction enzyme cleavage patterns. For example, sample and control DNA is isolated, amplified (optionally),  
10 digested with one or more restriction endonucleases, and fragment length sizes are determined by gel electrophoresis. Moreover, the use of sequence specific ribozymes (see, for example, U.S. Patent No. 5,498,531) can be used to score for the presence of specific mutations by development or loss of a ribozyme cleavage site.

15 4. *In situ* hybridization

In one aspect, the method comprises *in situ* hybridization with a probe derived from a given marker polynucleotide, which sequence is selected from any of the polynucleotide sequences of the SEQ ID NO: 1 to 165 or a sequence complementary thereto. The method comprises contacting the labeled hybridization probe with a  
20 sample of a given type of tissue from a patient potentially having malignant neoplasia and breast cancer in particular as well as normal tissue from a person with no malignant neoplasia, and determining whether the probe labels tissue of the patient to a degree significantly different (e.g., by at least a factor of two, or at least a  
25 factor of five, or at least a factor of twenty, or at least a factor of fifty) than the degree to which normal tissue is labelled.

Polypeptide detection

30 The subject invention further provides a method of determining whether a cell sample obtained from a subject possesses an abnormal amount of marker polypeptide

which comprises (a) obtaining a cell sample from the subject, (b) quantitatively determining the amount of the marker polypeptide in the sample so obtained, and (c) comparing the amount of the marker polypeptide so determined with a known standard, so as to thereby determine whether the cell sample obtained from the subject possesses an abnormal amount of the marker polypeptide. Such marker polypeptides may be detected by immunohistochemical assays, dot-blot assays, ELISA and the like.

### Antibodies

Any type of antibody known in the art can be generated to bind specifically to an epitope of a „BREAST CANCER GENE“ polypeptide. An antibody as used herein includes intact immunoglobulin molecules, as well as fragments thereof, such as Fab, F(ab)<sub>2</sub>, and Fv, which are capable of binding an epitope of a „BREAST CANCER GENE“ polypeptide. Typically, at least 6, 8, 10, or 12 contiguous amino acids are required to form an epitope. However, epitopes which involve non-contiguous amino acids may require more, e.g., at least 15, 25, or 50 amino acids.

An antibody which specifically binds to an epitope of a „BREAST CANCER GENE“ polypeptide can be used therapeutically, as well as in immunochemical assays, such as Western blots, ELISAs, radioimmunoassays, immunohistochemical assays, immunoprecipitations, or other immunochemical assays known in the art. Various immunoassays can be used to identify antibodies having the desired specificity. Numerous protocols for competitive binding or immunoradiometric assays are well known in the art. Such immunoassays typically involve the measurement of complex formation between an immunogen and an antibody which specifically binds to the immunogen.

Typically, an antibody which specifically binds to a „BREAST CANCER GENE“ polypeptide provides a detection signal at least 5-, 10-, or 20-fold higher than a detection signal provided with other proteins when used in an immunochemical

assay. Preferably, antibodies which specifically bind to „BREAST CANCER GENE“ polypeptides do not detect other proteins in immunochemical assays and can immunoprecipitate a „BREAST CANCER GENE“ polypeptide from solution.

5 „BREAST CANCER GENE“ polypeptides can be used to immunize a mammal, such as a mouse, rat, rabbit, guinea pig, monkey, or human, to produce polyclonal antibodies. If desired, a „BREAST CANCER GENE“ polypeptide can be conjugated to a carrier protein, such as bovine serum albumin, thyroglobulin, and keyhole limpet hemocyanin. Depending on the host species, various adjuvants can be used to  
10 increase the immunological response. Such adjuvants include, but are not limited to, Freund's adjuvant, mineral gels (e.g., aluminum hydroxide), and surface active substances (e.g. lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanin, and dinitrophenol). Among adjuvants used in humans, BCG (bacilli Calmette-Guerin) and Corynebacterium parvum are especially useful.

15 Monoclonal antibodies which specifically bind to a „BREAST CANCER GENE“ polypeptide can be prepared using any technique which provides for the production of antibody molecules by continuous cell lines in culture. These techniques include, but are not limited to, the hybridoma technique, the human B cell hybridoma  
20 technique, and the EBV hybridoma technique [Kohler et al., 1985, (65); Kozbor et al., 1985, (66); Cote et al., 1983, (67) and Cole et al., 1984, (68)].

In addition, techniques developed for the production of chimeric antibodies, the  
25 splicing of mouse antibody genes to human antibody genes to obtain a molecule with appropriate antigen specificity and biological activity, can be used [Morrison et al., 1984, (69); Neuberger et al., 1984, (70); Takeda et al., 1985, (71)]. Monoclonal and other antibodies also can be humanized to prevent a patient from mounting an immune response against the antibody when it is used therapeutically. Such anti-  
30 bodies may be sufficiently similar in sequence to human antibodies to be used directly in therapy or may require alteration of a few key residues. Sequence differences between rodent antibodies and human sequences can be minimized by

replacing residues which differ from those in the human sequences by site directed mutagenesis of individual residues or by grating of entire complementarity determining regions. Alternatively, humanized antibodies can be produced using recombinant methods, as described in GB2188638B. Antibodies which specifically bind to a „BREAST CANCER GENE“ polypeptide can contain antigen binding sites which are either partially or fully humanized, as disclosed in U.S. Patent 5,565,332.

Alternatively, techniques described for the production of single chain antibodies can be adapted using methods known in the art to produce single chain antibodies which specifically bind to „BREAST CANCER GENE“ polypeptides. Antibodies with related specificity, but of distinct idiotypic composition, can be generated by chain shuffling from random combinatorial immunoglobulin libraries [Burton, 1991, (72)].

Single-chain antibodies also can be constructed using a DNA amplification method, such as PCR, using hybridoma cDNA as a template [Thirion et al., 1996, (73)]. Single-chain antibodies can be mono- or bispecific, and can be bivalent or tetravalent. Construction of tetravalent, bispecific single-chain antibodies is taught, for example, in Coloma & Morrison, (74). Construction of bivalent, bispecific single-chain antibodies is taught in Mallender & Voss, (75).

A nucleotide sequence encoding a single-chain antibody can be constructed using manual or automated nucleotide synthesis, cloned into an expression construct using standard recombinant DNA methods, and introduced into a cell to express the coding sequence, as described below. Alternatively, single-chain antibodies can be produced directly using, for example, filamentous phage technology [Verhaar et al., 1995, (76); Nicholls et al., 1993, (77)].

Antibodies which specifically bind to „BREAST CANCER GENE“ polypeptides also can be produced by inducing in vivo production in the lymphocyte population or by screening immunoglobulin libraries or panels of highly specific binding reagents

as disclosed in the literature [Orlandi et al., 1989, (789) and Winter et al., 1991, (79)].

5 Other types of antibodies can be constructed and used therapeutically in methods of the invention. For example, chimeric antibodies can be constructed as disclosed in WO 93/03151. Binding proteins which are derived from immunoglobulins and which are multivalent and multispecific, such as the antibodies described in WO 94/13804, also can be prepared.

10 Antibodies according to the invention can be purified by methods well known in the art. For example, antibodies can be affinity purified by passage over a column to which a „BREAST CANCER GENE“ polypeptide is bound. The bound antibodies can then be eluted from the column using a buffer with a high salt concentration.

15 Immunoassays are commonly used to quantify the levels of proteins in cell samples, and many other immunoassay techniques are known in the art. The invention is not limited to a particular assay procedure, and therefore is intended to include both homogeneous and heterogeneous procedures. Exemplary immunoassays which can be conducted according to the invention include fluorescence polarisation immuno-  
20 assay (FPIA), fluorescence immunoassay (FIA), enzyme immunoassay (EIA), nephelometric inhibition immunoassay (NIA), enzyme linked immunosorbent assay (ELISA), and radioimmunoassay (RIA). An indicator moiety, or label group, can be attached to the subject antibodies and is selected so as to meet the needs of various uses of the method which are often dictated by the availability of assay equipment  
25 and compatible immunoassay procedures. General techniques to be used in performing the various immunoassays noted above are known to those of ordinary skill in the art.

30 Other methods to quantify the level of a particular protein, or a protein fragment, or modified protein in a particular sample are based on flow-cytometric methods. Flow cytometry allows the identification of proteins on the cell surface as well as of

intracellular proteins using fluorochrome labeled, protein specific antibodies or non-labeled antibodies in combination with fluorochrome labeled secondary antibodies. General techniques to be used in performing flow cytometric assays noted above are known to those of ordinary skill in the art. A special method based on the same principles is the microsphere-based flow cytometric. Microsphere beads are labeled with precise quantities of fluorescent dye and particular antibodies. Such techniques are provided by Luminex Inc. WO 97/14028. In another embodiment the level of a particular protein or a protein fragment, or modified protein in a particular sample may be determined by 2D gel-electrophoresis and/or mass spectrometry. Determination of protein nature, sequence, molecular mass as well charge can be achieved in one detection step. Mass spectrometry can be performed with methods known to those with skills in the art as MALDI, TOF, or combinations of these.

In another embodiment, the level of the encoded product, i.e., the product encoded by any of the polynucleotide sequences of the SEQ ID NO: 1 to 165 or a sequence complementary thereto, in a biological fluid (e.g., blood or urine) of a patient may be determined as a way of monitoring the level of expression of the marker polynucleotide sequence in cells of that patient. Such a method would include the steps of obtaining a sample of a biological fluid from the patient, contacting the sample (or proteins from the sample) with an antibody specific for a encoded marker polypeptide, and determining the amount of immune complex formation by the antibody, with the amount of immune complex formation being indicative of the level of the marker encoded product in the sample. This determination is particularly instructive when compared to the amount of immune complex formation by the same antibody in a control sample taken from a normal individual or in one or more samples previously or subsequently obtained from the same person.

In another embodiment, the method can be used to determine the amount of marker polypeptide present in a cell, which in turn can be correlated with progression of the disorder, e.g., plaque formation. The level of the marker polypeptide can be used predictively to evaluate whether a sample of cells contains cells which are, or are

predisposed towards becoming, plaque associated cells. The observation of marker polypeptide level can be utilized in decisions regarding, e.g., the use of more stringent therapies.

5 As set out above, one aspect of the present invention relates to diagnostic assays for determining, in the context of cells isolated from a patient, if the level of a marker polypeptide is significantly reduced in the sample cells. The term "significantly reduced" refers to a cell phenotype wherein the cell possesses a reduced cellular amount of the marker polypeptide relative to a normal cell of similar tissue origin.  
10 For example, a cell may have less than about 50%, 25%, 10%, or 5% of the marker polypeptide that a normal control cell. In particular, the assay evaluates the level of marker polypeptide in the test cells, and, preferably, compares the measured level with marker polypeptide detected in at least one control cell, e.g., a normal cell and/or a transformed cell of known phenotype.

15 Of particular importance to the subject invention is the ability to quantify the level of marker polypeptide as determined by the number of cells associated with a normal or abnormal marker polypeptide level. The number of cells with a particular marker polypeptide phenotype may then be correlated with patient prognosis. In one  
20 embodiment of the invention, the marker polypeptide phenotype of the lesion is determined as a percentage of cells in a biopsy which are found to have abnormally high/low levels of the marker polypeptide. Such expression may be detected by immunohistochemical assays, dot-blot assays, ELISA and the like.

#### 25 Immunohistochemistry

Where tissue samples are employed, immunohistochemical staining may be used to determine the number of cells having the marker polypeptide phenotype. For such staining, a multiblock of tissue is taken from the biopsy or other tissue sample and  
30 subjected to proteolytic hydrolysis, employing such agents as protease K or pepsin.



In certain embodiments, it may be desirable to isolate a nuclear fraction from the sample cells and detect the level of the marker polypeptide in the nuclear fraction.

5 The tissues samples are fixed by treatment with a reagent such as formalin, glutaraldehyde, methanol, or the like. The samples are then incubated with an antibody, preferably a monoclonal antibody, with binding specificity for the marker polypeptides. This antibody may be conjugated to a Label for subsequent detection of binding. samples are incubated for a time Sufficient for formation of the immuno-complexes. Binding of the antibody is then detected by virtue of a Label conjugated to this antibody. Where the antibody is unlabelled, a second labeled antibody may be employed, e.g., which is specific for the isotype of the anti-marker polypeptide anti-body. Examples of labels which may be employed include radionuclides, fluores-  
10 cence, chemoluminescence, and enzymes.

15 Where enzymes are employed, the Substrate for the enzyme may be added to the samples to provide a colored or fluorescent product. Examples of suitable enzymes for use in conjugates include horseradish peroxidase, alkaline phosphatase, malate dehydrogenase and the like. Where not commercially available, such antibody-enzyme conjugates are readily produced by techniques known to those skilled in the  
20 art.

In one embodiment, the assay is performed as a dot blot assay. The dot blot assay finds particular application where tissue samples are employed as it allows determination of the average amount of the marker polypeptide associated with a  
25 Single cell by correlating the amount of marker polypeptide in a cell-free extract produced from a predetermined number of cells.

In yet another embodiment, the invention contemplates using a panel of antibodies which are generated against the marker polypeptides of this invention, which  
30 polypeptides are encoded by any of the polynucleotide sequences of the SEQ ID NO: 1 to 165. Such a panel of antibodies may be used as a reliable diagnostic probe for

breast cancer. The assay of the present invention comprises contacting a biopsy sample containing cells, e.g., macrophages, with a panel of antibodies to one or more of the encoded products to determine the presence or absence of the marker polypeptides.

5

The diagnostic methods of the subject invention may also be employed as follow-up to treatment, e.g., quantification of the level of marker polypeptides may be indicative of the effectiveness of current or previously employed therapies for malignant neoplasia and breast cancer in particular as well as the effect of these therapies upon patient prognosis.

10

The diagnostic assays described above can be adapted to be used as prognostic assays, as well. Such an application takes advantage of the sensitivity of the assays of the Invention to events which take place at characteristic stages in the progression of plaque generation in case of malignant neoplasia. For example, a given marker gene may be up- or down-regulated at a very early stage, perhaps before the cell is developing into a foam cell, while another marker gene may be characteristically up or down regulated only at a much later stage. Such a method could involve the steps of contacting the mRNA of a test cell with a polynucleotide probe derived from a given marker polynucleotide which is expressed at different characteristic levels in breast cancer tissue cells at different stages of malignant neoplasia progression, and determining the approximate amount of hybridization of the probe to the mRNA of the cell, such amount being an indication of the level of expression of the gene in the cell, and thus an indication of the stage of disease progression of the cell; alternatively, the assay can be carried out with an antibody specific for the gene product of the given marker polynucleotide, contacted with the proteins of the test cell. A battery of such tests will disclose not only the existence of a certain neoplastic lesion, but also will allow the clinician to select the mode of treatment most appropriate for the disease, and to predict the likelihood of success of that treatment.

25  
30

The methods of the invention can also be used to follow the clinical course of a given breast cancer predisposition. For example, the assay of the Invention can be applied to a blood sample from a patient; following treatment of the patient for BREAST CANCER, another blood sample is taken and the test repeated. Successful treatment will result in removal of demonstrate differential expression, characteristic of the breast cancer tissue cells, perhaps approaching or even surpassing normal levels.

Polypeptide activity

- 10 In one embodiment the present invention provides a method for screening potentially therapeutic agents which modulate the activity of one or more "BREAST CANCER GENE" polypeptides, such that if the activity of the polypeptide is increased as a result of the upregulation of the "BREAST CANCER GENE" in a subject having or at risk for malignant neoplasia and breast cancer in particular, the therapeutic
- 15 substance will decrease the activity of the polypeptide relative to the activity of the some polypeptide in a subject not having or not at risk for malignant neoplasia or breast cancer in particular but not treated with the therapeutic agent. Likewise, if the activity of the polypeptide as a result of the downregulation of the "BREAST CANCER GENE" is decreased in a subject having or at risk for malignant neoplasia or breast cancer in particular, the therapeutic agent will increase the activity of the
- 20 polypeptide relative to the activity of the same polypeptide in a subject not having or not at risk for malignant neoplasia or breast cancer in particular, but not treated with the therapeutic agent.
- 25 The activity of the "BREAST CANCER GENE" polypeptides indicated in Table 2 or 3 may be measured by any means known to those of skill in the art, and which are particular for the type of activity performed by the particular polypeptide. Examples of specific assays which may be used to measure the activity of particular polynucleotides are shown below.

a) G protein coupled receptors

In one embodiment, the "BREAST CANCER GENE" polynucleotide may encode a G protein coupled receptor. In one embodiment, the present invention provides a method of screening potential modulators (inhibitors or activators) of the G protein coupled receptor by measuring changes in the activity of the receptor in the presence of a candidate modulator.

1)  $G_i$ -coupled receptors

Cells (such as CHO cells or primary cells) are stably transfected with the relevant receptor and with an inducible CRE-luciferase construct. Cells are grown in 50% Dulbecco's modified Eagle medium / 50% F12 (DMEM/F12) supplemented with 10% FBS, at 37°C in a humidified atmosphere with 10% CO<sub>2</sub> and are routinely split at a ratio of 1:10 every 2 or 3 days. Test cultures are seeded into 384 – well plates at an appropriate density (e.g. 2000 cells / well in 35 µl cell culture medium) in DMEM/F12 with FBS, and are grown for 48 hours (range: ~ 24 - 60 hours, depending on cell line). Growth medium is then exchanged against serum free medium (SFM; e.g. Ultra-CHO), containing 0,1% BSA. Test compounds dissolved in DMSO are diluted in SFM and transferred to the test cultures (maximal final concentration 10 µmolar), followed by addition of forskolin (~ 1 µmolar, final conc.) in SFM + 0,1% BSA 10 minutes later. In case of antagonist screening both, an appropriate concentration of agonist, and forskolin are added. The plates are incubated at 37°C in 10% CO<sub>2</sub> for 3 hours. Then the supernatant is removed, cells are lysed with lysis reagent (25 mmolar phosphate-buffer, pH 7,8, containing 2 mmolar DDT, 10% glycerol and 3% Triton X100). The luciferase reaction is started by addition of substrate-buffer (e.g. luciferase assay reagent, Promega) and luminescence is immediately determined (e.g. Berthold luminometer or Hamamatsu camera system).

2)  $G_s$ -coupled receptors

Cells (such as CHO cells or primary cells) are stably transfected with the relevant receptor and with an inducible CRE-luciferase construct. Cells are grown in 50% Dulbecco's modified Eagle medium / 50% F12 (DMEM/F12) supplemented with 10% FBS, at 37°C in a humidified atmosphere with 10% CO<sub>2</sub> and are routinely split at a ratio of 1:10 every 2 or 3 days. Test cultures are seeded into 384 – well plates at an appropriate density (e.g. 1000 or 2000 cells / well in 35 µl cell culture medium) in DMEM/F12 with FBS, and are grown for 48 hours (range: ~ 24 - 60 hours, depending on cell line). The assay is started by addition of test-compounds in serum free medium (SFM; e.g. Ultra-CHO) containing 0,1% BSA: Test compounds are dissolved in DMSO, diluted in SFM and transferred to the test cultures (maximal final concentration 10 µmolar, DMSO conc. < 0,6 %). In case of antagonist screening an appropriate concentration of agonist is added 5 – 10 minutes later. The plates are incubated at 37°C in 10% CO<sub>2</sub> for 3 hours. Then the cells are lysed with 10 µl lysis reagent per well (25 mmolar phosphate-buffer, pH 7,8 , containing 2 mmolar DDT, 10% glycerol and 3% Triton X100) and the luciferase reaction is started by addition of 20 µl substrate-buffer per well (e.g. luciferase assay reagent, Promega). Measurement of luminescence is started immediately (e.g. Berthold luminometer or Hamamatzu camera system).

3)  $G_q$ -coupled receptors

Cells (such as CHO cells or primary cells) are stably transfected with the relevant receptor. Cells expressing functional receptor protein are grown in 50% Dulbecco's modified Eagle medium / 50% F12 (DMEM/F12) supplemented with 10% FBS, at 37°C in a humidified atmosphere with 5% CO<sub>2</sub> and are routinely split at a cell line dependent ratio every 3 or 4 days. Test cultures are seeded into 384 – well plates at an appropriate density (e.g. 2000 cells / well in 35 µl cell culture medium) in DMEM/F12 with FBS, and are grown for 48 hours (range: ~ 24 - 60 hours, depending on cell line). Growth medium is then exchanged against physiological salt

5 solution (e.g. Tyrode solution). Test compounds dissolved in DMSO are diluted in Tyrode solution containing 0.1% BSA and transferred to the test cultures (maximal final concentration 10  $\mu$ molar). After addition of the receptor specific agonist the resulting Gq-mediated intracellular calcium increase is measured using appropriate read-out systems (e.g. calcium-sensitive dyes).

b) Ion channels

10 Ion channels are integral membrane proteins involved in electrical signaling, transmembrane signal transduction, and electrolyte and solute transport. By forming macromolecular pores through the membrane lipid bilayer, ion channels account for the flow of specific ion species driven by the electrochemical potential gradient for the permeating ion. At the single molecule level, individual channels undergo conformational transitions ("gating") between the 'open' (ion conducting) and 'closed' (non conducting) state. Typical single channel openings last for a few milliseconds and result in elementary transmembrane currents in the range of  $10^{-9}$  -  $10^{-12}$  Ampere. Channel gating is controlled by various chemical and/or biophysical parameters, such as neurotransmitters and intracellular second messengers ('ligand-gated' channels) or membrane potential ('voltage-gated' channels). Ion channels are functionally characterized by their ion selectivity, gating properties, and regulation by hormones and pharmacological agents. Because of their central role in signaling and transport processes, ion channels present ideal targets for pharmacological therapeutics in various pathophysiological settings.

25 In one embodiment, the "BREAST CANCER GENE" may encode an ion channel. In one embodiment, the present invention provides a method of screening potential activators or inhibitors of channels activity of the "BREAST CANCER GENE" polypeptide. Screening for compounds interaction with ion channels to either inhibit or promote their activity can be based on (1.) binding and (2.) functional assays in living cells[ Hille (112)].

30

1. For ligand-gated channels, e.g. ionotropic neurotransmitter/hormone receptors, assays can be designed detecting binding to the target by competition between the compound and a labeled ligand.
2. Ion channel function can be tested functionally in living cells. Target proteins are either expressed endogenously in appropriate reporter cells or are introduced recombinantly. Channel activity can be monitored by (2.1) concentration changes of the permeating ion (most prominently  $\text{Ca}^{2+}$  ions), (2.2) by changes in the transmembrane electrical potential gradient, and (2.3) by measuring a cellular response (e.g. expression of a reporter gene, secretion of a neurotransmitter) triggered or modulated by the target activity.
  - 2.1 Channel activity results in transmembrane ion fluxes. Thus activation of ionic channels can be monitored by the resulting changes in intracellular ion concentrations using luminescent or fluorescent indicators. Because of its wide dynamic range and availability of suitable indicators this applies particularly to changes in intracellular  $\text{Ca}^{2+}$  ion concentration ( $[\text{Ca}^{2+}]_i$ ).  $[\text{Ca}^{2+}]_i$  can be measured, for example, by aequorin luminescence or fluorescence dye technology (e.g. using Fluo-3, Indo-1, Fura-2). Cellular assays can be designed where either the  $\text{Ca}^{2+}$  flux through the target channel itself is measured directly or where modulation of the target channel affects membrane potential and thereby the activity of co-expressed voltage-gated  $\text{Ca}^{2+}$  channels.
  - 2.2 Ion channel currents result in changes of electrical membrane potential ( $V_m$ ) which can be monitored directly using potentiometric fluorescent probes. These electrically charged indicators (e.g. the anionic oxonol dye DiBAC<sub>4</sub>(3)) redistribute between extra- and intracellular compartment in response to voltage changes. The equilibrium distribution is governed by the Nernst-equation. Thus changes in membrane potential results in concomitant changes in cellular fluorescence. Again, changes in  $V_m$  might be caused directly by the

activity of the target ion channel or through amplification and/or prolongation of the signal by channels co-expressed in the same cell.

- 2.3 Target channel activity can cause cellular  $\text{Ca}^{2+}$  entry either directly or through activation of additional  $\text{Ca}^{2+}$  channel (see 2.1). The resulting intracellular  $\text{Ca}^{2+}$  signals regulate a variety of cellular responses, e.g. secretion or gene transcription. Therefore modulation of the target channel can be detected by monitoring secretion of a known hormone/transmitter from the target-expressing cell or through expression of a reporter gene (e.g. luciferase) controlled by an  $\text{Ca}^{2+}$ -responsive promoter element (e.g. cyclic AMP/  $\text{Ca}^{2+}$ -responsive elements; CRE).

c) DNA-binding proteins and transcription factors

- 15 In one embodiment, the "BREAST CANCER GENE" may encode a DNA-binding protein or a transcription factor. The activity of such a DNA-binding protein or a transcription factor may be measured, for example, by a promoter assay which measures the ability of the DNA-binding protein or the transcription factor to initiate transcription of a test sequence linked to a particular promoter. In one embodiment,
- 20 the present invention provides a method of screening test compounds for its ability to modulate the activity of such a DNA-binding protein or a transcription factor by measuring the changes in the expression of a test gene which is regulated by a promoter which is responsive to the transcription factor.

25 Promotor assays

- A promoter assay was set up with a human hepatocellular carcinoma cell HepG2 that was stably transfected with a luciferase gene under the control of a gene of interest (e.g. thyroid hormone) regulated promoter. The vector 2xIROluc, which was used for
- 30 transfection, carries a thyroid hormone responsive element (TRE) of two 12 bp inverted palindromes separated by an 8 bp spacer in front of a tk minimal promoter



and the luciferase gene. Test cultures were seeded in 96 well plates in serum - free Eagle's Minimal Essential Medium supplemented with glutamine, tricine, sodium pyruvate, non - essential amino acids, insulin, selen, transferrin, and were cultivated in a humidified atmosphere at 10 % CO<sub>2</sub> at 37°C. After 48 hours of incubation serial dilutions of test compounds or reference compounds (L-T3, L-T4 e.g.) and co-stimulator if appropriate (final concentration 1 nM) were added to the cell cultures and incubation was continued for the optimal time (e.g. another 4-72 hours). The cells were then lysed by addition of buffer containing Triton X100 and luciferin and the luminescence of luciferase induced by T3 or other compounds was measured in a luminometer. For each concentration of a test compound replicates of 4 were tested. EC<sub>50</sub> - values for each test compound were calculated by use of the Graph Pad Prism Scientific software.

#### Screening Methods

The invention provides assays for screening test compounds which bind to or modulate the activity of a „BREAST CANCER GENE“ polypeptide or a „BREAST CANCER GENE“ polynucleotide. A test compound preferably binds to a „BREAST CANCER GENE“ polypeptide or polynucleotide. More preferably, a test compound decreases or increases „BREAST CANCER GENE“ activity by at least about 10, preferably about 50, more preferably about 75, 90, or 100% relative to the absence of the test compound.

#### Test Compounds

Test compounds can be pharmacological agents already known in the art or can be compounds previously unknown to have any pharmacological activity. The compounds can be naturally occurring or designed in the laboratory. They can be isolated from microorganisms, animals, or plants, and can be produced recombinant, or synthesised by chemical methods known in the art. If desired, test compounds can be obtained using any of the numerous combinatorial library methods known in the

art, including but not limited to, biological libraries, spatially addressable parallel solid phase or solution phase libraries, synthetic library methods requiring deconvolution, the one-bead one-compound library method, and synthetic library methods using affinity chromatography selection. The biological library approach is limited to polypeptide libraries, while the other four approaches are applicable to polypeptide, non-peptide oligomer, or small molecule libraries of compounds. [For review see Lam, 1997, (80)].

Methods for the synthesis of molecular libraries are well known in the art [see, for example, DeWitt et al., 1993, (81); Erb et al., 1994, (82); Zuckermann et al., 1994, (83); Cho et al., 1993, (84); Carell et al., 1994, (85) and Gallop et al., 1994, (86). Libraries of compounds can be presented in solution [see, e.g., Houghten, 1992, (87)], or on beads [Lam, 1991, (88)], DNA-chips [Fodor, 1993, (89)], bacteria or spores (Ladner, U.S. Patent 5,223,409), plasmids [Cull et al., 1992, (90)], or phage [Scott & Smith, 1990, (91); Devlin, 1990, (92); Cwirla et al., 1990, (93); Felici, 1991, (94)].

#### High Throughput Screening

Test compounds can be screened for the ability to bind to „BREAST CANCER GENE“ polypeptides or polynucleotides or to affect „BREAST CANCER GENE“ activity or „BREAST CANCER GENE“ expression using high throughput screening. Using high throughput screening, many discrete compounds can be tested in parallel so that large numbers of test compounds can be quickly screened. The most widely established techniques utilize 96-well, 384-well or 1536-well microtiter plates. The wells of the microtiter plates typically require assay volumes that range from 5 to 500 µl. In addition to the plates, many instruments, materials, pipettors, robotics, plate washers, and plate readers are commercially available to fit the microwell formats.

Alternatively, free format assays, or assays that have no physical barrier between samples, can be used. For example, an assay using pigment cells (melanocytes) in a

simple homogeneous assay for combinatorial peptide libraries is described by Jayawickreme et al., (95). The cells are placed under agarose in culture dishes, then beads that carry combinatorial compounds are placed on the surface of the agarose. The combinatorial compounds are partially released the compounds from the beads. Active compounds can be visualised as dark pigment areas because, as the compounds diffuse locally into the gel matrix, the active compounds cause the cells to change colors.

Another example of a free format assay is described by Chelsky, (96). Chelsky placed a simple homogenous enzyme assay for carbonic anhydrase inside an agarose gel such that the enzyme in the gel would cause a color change throughout the gel. Thereafter, beads carrying combinatorial compounds via a photolinker were placed inside the gel and the compounds were partially released by UV light. Compounds that inhibited the enzyme were observed as local zones of inhibition having less color change.

In another example, combinatorial libraries were screened for compounds that had cytotoxic effects on cancer cells growing in agar [Salmon et al., 1996, (97)].

Another high throughput screening method is described in Beutel et al., U.S. Patent 5,976,813. In this method, test samples are placed in a porous matrix. One or more assay components are then placed within, on top of, or at the bottom of a matrix such as a gel, a plastic sheet, a filter, or other form of easily manipulated solid support. When samples are introduced to the porous matrix they diffuse sufficiently slowly, such that the assays can be performed without the test samples running together.

#### Binding Assays

For binding assays, the test compound is preferably a small molecule which binds to and occupies, for example, the ATP/GTP binding site of the enzyme or the active site of a „BREAST CANCER GENE“ polypeptide, such that normal biological activity

is prevented. Examples of such small molecules include, but are not limited to, small peptides or peptide-like molecules.

5 In binding assays, either the test compound or a „BREAST CANCER GENE“ polypeptide can comprise a detectable label, such as a fluorescent, radioisotopic, chemiluminescent, or enzymatic label, such as horseradish peroxidase, alkaline phosphatase, or luciferase. Detection of a test compound which is bound to a „BREAST CANCER GENE“ polypeptide can then be accomplished, for example, by direct counting of radioemmission, by scintillation counting, or by determining  
10 conversion of an appropriate substrate to a detectable product.

Alternatively, binding of a test compound to a „BREAST CANCER GENE“ polypeptide can be determined without labeling either of the interactants. For example, a microphysiometer can be used to detect binding of a test compound with a  
15 „BREAST CANCER GENE“ polypeptide. A microphysiometer (e.g., CytosensorJ) is an analytical instrument that measures the rate at which a cell acidifies its environment using a light-addressable potentiometric sensor (LAPS). Changes in this acidification rate can be used as an indicator of the interaction between a test compound and a „BREAST CANCER GENE“ polypeptide [McConnell et al., 1992,  
20 (98)].

Determining the ability of a test compound to bind to a „BREAST CANCER GENE“ polypeptide also can be accomplished using a technology such as real-time Bimolecular Interaction Analysis (BIA) [Sjolander & Urbaniczky, 1991, (99), and  
25 Szabo et al., 1995, (100)]. BIA is a technology for studying biospecific interactions in real time, without labeling any of the interactants (e.g., BIAcore™). Changes in the optical phenomenon surface plasmon resonance (SPR) can be used as an indication of real-time reactions between biological molecules.

30 In yet another aspect of the invention, a „BREAST CANCER GENE“ polypeptide can be used as a "bait protein" in a two-hybrid assay or three-hybrid assay [see, e.g.,

U.S. Patent 5,283,317; Zervos et al., 1993, (101); Madura et al., 1993, (102); Bartel et al., 1993, (1034); Iwabuchi et al., 1993, (104) and Brent WO 94/10300], to identify other proteins which bind to or interact with the „BREAST CANCER GENE“ polypeptide and modulate its activity.

5

10 The two-hybrid system is based on the modular nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. For example, in one construct, polynucleotide encoding a „BREAST CANCER GENE“ polypeptide can be fused to a polynucleotide encoding the DNA binding domain of a known transcription factor (e.g., GAL4). In the other construct a DNA sequence that encodes an unidentified protein ("prey" or "sample") can be fused to a polynucleotide that codes for the activation domain of the known transcription factor. If the "bait" and the "prey" proteins are able to interact in vivo to form an protein- dependent complex, the DNA-binding and activation domains of the transcription factor are brought into close proximity. This proximity allows transcription of a reporter gene (e.g., LacZ), which is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be detected, and cell colonies containing the functional transcription factor can be isolated and used to obtain the DNA sequence encoding the protein which interacts with the „BREAST CANCER GENE“ polypeptide.

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25 It may be desirable to immobilize either a „BREAST CANCER GENE“ polypeptide (or polynucleotide) or the test compound to facilitate separation of bound from unbound forms of one or both of the interactants, as well as to accommodate automation of the assay. Thus, either a „BREAST CANCER GENE“ polypeptide (or polynucleotide) or the test compound can be bound to a solid support. Suitable solid supports include, but are not limited to, glass or plastic slides, tissue culture plates, microtiter wells, tubes, silicon chips, or particles such as beads (including, but not limited to, latex, polystyrene, or glass beads). Any method known in the art can be used to attach a „BREAST CANCER GENE“ polypeptide (or polynucleotide) or test

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compound to a solid support, including use of covalent and non-covalent linkages, passive absorption, or pairs of binding moieties attached respectively to the polypeptide (or polynucleotide) or test compound and the solid support. Test compounds are preferably bound to the solid support in an array, so that the location of individual  
5 test compounds can be tracked. Binding of a test compound to a „BREAST CANCER GENE“ polypeptide (or polynucleotide) can be accomplished in any vessel suitable for containing the reactants. Examples of such vessels include microtiter plates, test tubes, and microcentrifuge tubes.

10 In one embodiment, a „BREAST CANCER GENE“ polypeptide is a fusion protein comprising a domain that allows the „BREAST CANCER GENE“ polypeptide to be bound to a solid support. For example, glutathione S-transferase fusion proteins can be adsorbed onto glutathione sepharose beads (Sigma Chemical, St. Louis, Mo.) or glutathione derivatized microtiter plates, which are then combined with the test  
15 compound or the test compound and the nonadsorbed „BREAST CANCER GENE“ polypeptide; the mixture is then incubated under conditions conducive to complex formation (e.g., at physiological conditions for salt and pH). Following incubation, the beads or microtiter plate wells are washed to remove any unbound components. Binding of the interactants can be determined either directly or indirectly, as  
20 described above. Alternatively, the complexes can be dissociated from the solid support before binding is determined.

Other techniques for immobilising proteins or polynucleotides on a solid support also can be used in the screening assays of the invention. For example, either a „BREAST  
25 CANCER GENE“ polypeptide (or polynucleotide) or a test compound can be immobilized utilizing conjugation of biotin and streptavidin. Biotinylated „BREAST CANCER GENE“ polypeptides (or polynucleotides) or test compounds can be prepared from biotin NHS (N-hydroxysuccinimide) using techniques well known in the art (e.g., biotinylation kit, Pierce Chemicals, Rockford, Ill.) and immobilized in  
30 the wells of streptavidin-coated 96 well plates (Pierce Chemical). Alternatively, antibodies which specifically bind to a „BREAST CANCER GENE“ polypeptide,

polynucleotide, or a test compound, but which do not interfere with a desired binding site, such as the ATP/GTP binding site or the active site of the „BREAST CANCER GENE“ polypeptide, can be derivatised to the wells of the plate. Unbound target or protein can be trapped in the wells by antibody conjugation.

5

Methods for detecting such complexes, in addition to those described above for the GST-immobilized complexes, include immunodetection of complexes using antibodies which specifically bind to a „BREAST CANCER GENE“ polypeptide or test compound, enzyme-linked assays which rely on detecting an activity of a „BREAST CANCER GENE“ polypeptide, and SDS gel electrophoresis under non-reducing conditions.

10

Screening for test compounds which bind to a „BREAST CANCER GENE“ polypeptide or polynucleotide also can be carried out in an intact cell. Any cell which comprises a „BREAST CANCER GENE“ polypeptide or polynucleotide can be used in a cell-based assay system. A „BREAST CANCER GENE“ polynucleotide can be naturally occurring in the cell or can be introduced using techniques such as those described above. Binding of the test compound to a „BREAST CANCER GENE“ polypeptide or polynucleotide is determined as described above.

15

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#### Modulation of Gene Expression

In another embodiment, test compounds which increase or decrease „BREAST CANCER GENE“ expression are identified. A „BREAST CANCER GENE“ polynucleotide is contacted with a test compound in an appropriate expression test system as described below or in a cell system, and the expression of an RNA or polypeptide product of the „BREAST CANCER GENE“ polynucleotide is determined. The level of expression of appropriate mRNA or polypeptide in the presence of the test compound is compared to the level of expression of mRNA or polypeptide in the absence of the test compound. The test compound can then be identified as a modulator of expression based on this comparison. For example, when expression of

25

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mRNA or polypeptide is greater in the presence of the test compound than in its absence, the test compound is identified as a stimulator or enhancer of the mRNA or polypeptide expression. Alternatively, when expression of the mRNA or polypeptide is less in the presence of the test compound than in its absence, the test compound is identified as an inhibitor of the mRNA or polypeptide expression.

The level of „BREAST CANCER GENE“ mRNA or polypeptide expression in the cells can be determined by methods well known in the art for detecting mRNA or polypeptide. Either qualitative or quantitative methods can be used. The presence of polypeptide products of a „BREAST CANCER GENE“ polynucleotide can be determined, for example, using a variety of techniques known in the art, including immunochemical methods such as radioimmunoassay, Western blotting, and immunohistochemistry. Alternatively, polypeptide synthesis can be determined in vivo, in a cell culture, or in an in vitro translation system by detecting incorporation of labeled amino acids into a „BREAST CANCER GENE“ polypeptide.

Such screening can be carried out either in a cell-free assay system or in an intact cell. Any cell which expresses a „BREAST CANCER GENE“ polynucleotide can be used in a cell-based assay system. A „BREAST CANCER GENE“ polynucleotide can be naturally occurring in the cell or can be introduced using techniques such as those described above. Either a primary culture or an established cell line, such as CHO or human embryonic kidney 293 cells, can be used.

#### Therapeutic Indications and Methods

Therapies for treatment of breast cancer primarily relied upon effective chemotherapeutic drugs for intervention on the cell proliferation, cell growth or angiogenesis. The advent of genomics-driven molecular target identification has opened up the possibility of identifying new breast cancer-specific targets for therapeutic intervention that will provide safer, more effective treatments for malignant neoplasia patients and breast cancer patients in particular. Thus, newly discovered breast



cancer-associated genes and their products can be used as tools to develop innovative therapies. The identification of the Her2/neu receptor kinase presents exciting new opportunities for treatment of a certain subset of tumor patients as described before. Genes playing important roles in any of the physiological processes outlined above  
5 can be characterized as breast cancer targets. Genes or gene fragments identified through genomics can readily be expressed in one or more heterologous expression systems to produce functional recombinant proteins. These proteins are characterized in vitro for their biochemical properties and then used as tools in high-throughput molecular screening programs to identify chemical modulators of their biochemical  
10 activities. Modulators of target gene expression or protein activity can be identified in this manner and subsequently tested in cellular and in vivo disease models for therapeutic activity. Optimization of lead compounds with iterative testing in biological models and detailed pharmacokinetic and toxicological analyses form the basis for drug development and subsequent testing in humans.

15 This invention further pertains to the use of novel agents identified by the screening assays described above. Accordingly, it is within the scope of this invention to use a test compound identified as described herein in an appropriate animal model. For example, an agent identified as described herein (e.g., a modulating agent, an  
20 antisense polynucleotide molecule, a specific antibody, ribozyme, or a human „BREAST CANCER GENE“ polypeptide binding molecule) can be used in an animal model to determine the efficacy, toxicity, or side effects of treatment with such an agent. Alternatively, an agent identified as described herein can be used in an animal model to determine the mechanism of action of such an agent. Furthermore,  
25 this invention pertains to uses of novel agents identified by the above described screening assays for treatments as described herein.

A reagent which affects human „BREAST CANCER GENE“ activity can be administered to a human cell, either in vitro or in vivo, to reduce or increase human  
30 „BREAST CANCER GENE“ activity. The reagent preferably binds to an expression product of a human „BREAST CANCER GENE“. If the expression product is a

protein, the reagent is preferably an antibody. For treatment of human cells ex vivo, an antibody can be added to a preparation of stem cells which have been removed from the body. The cells can then be replaced in the same or another human body, with or without clonal propagation, as is known in the art.

5

In one embodiment, the reagent is delivered using a liposome. Preferably, the liposome is stable in the animal into which it has been administered for at least about 30 minutes, more preferably for at least about 1 hour, and even more preferably for at least about 24 hours. A liposome comprises a lipid composition that is capable of  
10 targeting a reagent, particularly a polynucleotide, to a particular site in an animal, such as a human. Preferably, the lipid composition of the liposome is capable of targeting to a specific organ of an animal, such as the lung, liver, spleen, heart brain, lymph nodes, and skin.

15

A liposome useful in the present invention comprises a lipid composition that is capable of fusing with the plasma membrane of the targeted cell to deliver its contents to the cell. Preferably, the transfection efficiency of a liposome is about 0.5  $\mu\text{g}$  of DNA per 16 nmol of liposome delivered to about  $10^6$  cells, more preferably about 1.0  $\mu\text{g}$  of DNA per 16 nmol of liposome delivered to about  $10^6$  cells, and even  
20 more preferably about 2.0  $\mu\text{g}$  of DNA per 16 nmol of liposome delivered to about  $10^6$  cells. Preferably, a liposome is between about 100 and 500 nm, more preferably between about 150 and 450 nm, and even more preferably between about 200 and 400 nm in diameter.

25

Suitable liposomes for use in the present invention include those liposomes usually used in, for example, gene delivery methods known to those of skill in the art. More preferred liposomes include liposomes having a polycationic lipid composition and/or liposomes having a cholesterol backbone conjugated to polyethylene glycol. Optionally, a liposome comprises a compound capable of targeting the liposome to a  
30 particular cell type, such as a cell-specific ligand exposed on the outer surface of the liposome.

Complexing a liposome with a reagent such as an antisense oligonucleotide or ribozyme can be achieved using methods which are standard in the art (see, for example, U.S. Patent 5,705,151). Preferably, from about 0.1  $\mu\text{g}$  to about 10  $\mu\text{g}$  of polynucleotide is combined with about 8 nmol of liposomes, more preferably from about 0.5  $\mu\text{g}$  to about 5  $\mu\text{g}$  of polynucleotides are combined with about 8 nmol liposomes, and even more preferably about 1.0  $\mu\text{g}$  of polynucleotides is combined with about 8 nmol liposomes.

In another embodiment, antibodies can be delivered to specific tissues in vivo using receptor-mediated targeted delivery. Receptor-mediated DNA delivery techniques are taught in, for example, Findeis et al., 1993, (105); Chiou et al., 1994, (106); Wu & Wu, 1988, (107); Wu et al., 1994, (108); Zenke et al., 1990, (109); Wu et al., 1991, (110).

#### Determination of a Therapeutically Effective Dose

The determination of a therapeutically effective dose is well within the capability of those skilled in the art. A therapeutically effective dose refers to that amount of active ingredient which increases or decreases human „BREAST CANCER GENE“ activity relative to the human „BREAST CANCER GENE“ activity which occurs in the absence of the therapeutically effective dose.

For any compound, the therapeutically effective dose can be estimated initially either in cell culture assays or in animal models, usually mice, rabbits, dogs, or pigs. The animal model also can be used to determine the appropriate concentration range and route of administration. Such information can then be used to determine useful doses and routes for administration in humans.

Therapeutic efficacy and toxicity, e.g.,  $\text{ED}_{50}$  (the dose therapeutically effective in 50% of the population) and  $\text{LD}_{50}$  (the dose lethal to 50% of the population), can be

determined by standard pharmaceutical procedures in cell cultures or experimental animals. The dose ratio of toxic to therapeutic effects is the therapeutic index, and it can be expressed as the ratio,  $LD_{50}/ED_{50}$ .

5      Pharmaceutical compositions which exhibit large therapeutic indices are preferred. The data obtained from cell culture assays and animal studies is used in formulating a range of dosage for human use. The dosage contained in such compositions is preferably within a range of circulating concentrations that include the  $ED_{50}$  with little or no toxicity. The dosage varies within this range depending upon the dosage  
10      form employed, sensitivity of the patient, and the route of administration.

The exact dosage will be determined by the practitioner, in light of factors related to the subject that requires treatment. Dosage and administration are adjusted to provide sufficient levels of the active ingredient or to maintain the desired effect. Factors  
15      which can be taken into account include the severity of the disease state, general health of the subject, age, weight, and gender of the subject, diet, time and frequency of administration, drug combination(s), reaction sensitivities, and tolerance/response to therapy. Long-acting pharmaceutical compositions can be administered every 3 to 4 days, every week, or once every two weeks depending on the half-life and  
20      clearance rate of the particular formulation.

Normal dosage amounts can vary from 0.1 to 100,000 micrograms, up to a total dose of about 1 g, depending upon the route of administration. Guidance as to particular dosages and methods of delivery is provided in the literature and generally available  
25      to practitioners in the art. Those skilled in the art will employ different formulations for nucleotides than for proteins or their inhibitors. Similarly, delivery of polynucleotides or polypeptides will be specific to particular cells, conditions, locations, etc.

30      If the reagent is a single-chain antibody, polynucleotides encoding the antibody can be constructed and introduced into a cell either ex vivo or in vivo using well-

established techniques including, but not limited to, transferrin-polycation-mediated DNA transfer, transfection with naked or encapsulated nucleic acids, liposome-mediated cellular fusion, intracellular transportation of DNA-coated latex beads, protoplast fusion, viral infection, electroporation, a gene gun, and DEAE- or calcium phosphate-mediated transfection.

Effective in vivo dosages of an antibody are in the range of about 5  $\mu$ g to about 50  $\mu$ g/kg, about 50  $\mu$ g to about 5 mg/kg, about 100  $\mu$ g to about 500  $\mu$ g/kg of patient body weight, and about 200 to about 250  $\mu$ g/kg of patient body weight. For administration of polynucleotides encoding single-chain antibodies, effective in vivo dosages are in the range of about 100 ng to about 200 ng, 500 ng to about 50 mg, about 1  $\mu$ g to about 2 mg, about 5  $\mu$ g to about 500  $\mu$ g, and about 20  $\mu$ g to about 100  $\mu$ g of DNA.

If the expression product is mRNA, the reagent is preferably an antisense oligonucleotide or a ribozyme. Polynucleotides which express antisense oligonucleotides or ribozymes can be introduced into cells by a variety of methods, as described above.

Preferably, a reagent reduces expression of a „BREAST CANCER GENE“ gene or the activity of a „BREAST CANCER GENE“ polypeptide by at least about 10, preferably about 50, more preferably about 75, 90, or 100% relative to the absence of the reagent. The effectiveness of the mechanism chosen to decrease the level of expression of a „BREAST CANCER GENE“ gene or the activity of a „BREAST CANCER GENE“ polypeptide can be assessed using methods well known in the art, such as hybridization of nucleotide probes to „BREAST CANCER GENE“-specific mRNA, quantitative RT-PCR, immunologic detection of a „BREAST CANCER GENE“ polypeptide, or measurement of „BREAST CANCER GENE“ activity.

In any of the embodiments described above, any of the pharmaceutical compositions of the invention can be administered in combination with other appropriate thera-

peutic agents. Selection of the appropriate agents for use in combination therapy can be made by one of ordinary skill in the art, according to conventional pharmaceutical principles. The combination of therapeutic agents can act synergistically to effect the treatment or prevention of the various disorders described above. Using this  
5 approach, one may be able to achieve therapeutic efficacy with lower dosages of each agent, thus reducing the potential for adverse side effects.

Any of the therapeutic methods described above can be applied to any subject in need of such therapy, including, for example, birds and mammals such as dogs, cats,  
10 cows, pigs, sheep, goats, horses, rabbits, monkeys, and most preferably, humans.

All patents and patent applications cited in this disclosure are expressly incorporated herein by reference. The above disclosure generally describes the present invention. A more complete understanding can be obtained by reference to the following  
15 specific examples which are provided for purposes of illustration only and are not intended to limit the scope of the invention.

#### Pharmaceutical Compositions

20 The invention also provides pharmaceutical compositions which can be administered to a patient to achieve a therapeutic effect. Pharmaceutical compositions of the invention can comprise, for example, a „BREAST CANCER GENE“ polypeptide, „BREAST CANCER GENE“ polynucleotide, ribozymes or antisense oligonucleotides, antibodies which specifically bind to a „BREAST CANCER GENE“ poly-  
25 peptide, or mimetics, agonists, antagonists, or inhibitors of a „BREAST CANCER GENE“ polypeptide activity. The compositions can be administered alone or in combination with at least one other agent, such as stabilizing compound, which can be administered in any sterile, biocompatible pharmaceutical carrier, including, but not limited to, saline, buffered saline, dextrose, and water. The compositions can be  
30 administered to a patient alone, or in combination with other agents, drugs or hormones.

In addition to the active ingredients, these pharmaceutical compositions can contain suitable pharmaceutically acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. Pharmaceutical compositions of the invention can be administered by any number of routes including, but not limited to, oral, intravenous, intramuscular, intraarterial, intramedullary, intrathecal, intraventricular, transdermal, subcutaneous, intraperitoneal, intranasal, parenteral, topical, sublingual, or rectal means. Pharmaceutical compositions for oral administration can be formulated using pharmaceutically acceptable carriers well known in the art in dosages suitable for oral administration. Such carriers enable the pharmaceutical compositions to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions, and the like, for ingestion by the patient.

Pharmaceutical preparations for oral use can be obtained through combination of active compounds with solid excipient, optionally grinding a resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients are carbohydrate or protein fillers, such as sugars, including lactose, sucrose, mannitol, or sorbitol; starch from corn, wheat, rice, potato, or other plants; cellulose, such as methyl cellulose, hydroxypropylmethylcellulose, or sodium carboxymethylcellulose; gums including arabic and tragacanth; and proteins such as gelatin and collagen. If desired, disintegrating or solubilizing agents can be added, such as the cross-linked polyvinyl pyrrolidone, agar, alginic acid, or a salt thereof, such as sodium alginate.

Dragee cores can be used in conjunction with suitable coatings, such as concentrated sugar solutions, which also can contain gum arabic, talc, polyvinylpyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments can be added to the tablets or dragee coatings for product identification or to characterize the quantity of active compound, i.e., dosage.

Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a coating, such as glycerol or sorbitol. Push-fit capsules can contain active ingredients mixed with a  
5 filler or binders, such as lactose or starches, lubricants, such as talc or magnesium stearate, and, optionally, stabilizers. In soft capsules, the active compounds can be dissolved or suspended in suitable liquids, such as fatty oils, liquid, or liquid polyethylene glycol with or without stabilizers.

10 Pharmaceutical formulations suitable for parenteral administration can be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks' solution, Ringer's solution, or physiologically buffered saline. Aqueous injection  
15 suspensions can contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Additionally, suspensions of the active compounds can be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame  
20 oil, or synthetic fatty acid esters, such as ethyl oleate or triglycerides, or liposomes. Non-lipid polycationic amino polymers also can be used for delivery. Optionally, the suspension also can contain suitable stabilizers or agents which increase the solubility of the compounds to allow for the preparation of highly concentrated  
25 solutions. For topical or nasal administration, penetrants appropriate to the particular barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

25 The pharmaceutical compositions of the present invention can be manufactured in a manner that is known in the art, e.g., by means of conventional mixing, dissolving, granulating, dragee making, levigating, emulsifying, encapsulating, entrapping, or lyophilizing processes. The pharmaceutical composition can be provided as a salt and can be formed with many acids, including but not limited to, hydrochloric, sulfuric,  
30 acetic, lactic, tartaric, malic, succinic, etc. Salts tend to be more soluble in aqueous or other protonic solvents than are the corresponding free base forms. In other cases, the



preferred preparation can be a lyophilized powder which can contain any or all of the following: 150 mM histidine, 0.1%2% sucrose, and 27% mannitol, at a pH range of 4.5 to 5.5, that is combined with buffer prior to use.

5 Further details on techniques for formulation and administration can be found in the latest edition of REMINGTON'S PHARMACEUTICAL SCIENCES (111). After pharmaceutical compositions have been prepared, they can be placed in an appropriate container and labeled for treatment of an indicated condition. Such labeling would include amount, frequency, and method of administration.

10 One strategy for identifying genes that are involved in breast cancer is to detect genes that are expressed differentially under conditions associated with the disease versus non-disease or in the context of therapy response conditions. The sub-sections below describe a number of experimental systems which can be used to detect such  
15 differentially expressed genes. In general, these experimental systems include at least one experimental condition in which subjects or samples are treated in a manner associated with breast cancer, in addition to at least one experimental control condition lacking such disease associated treatment or does not respond to such treatment. Differentially expressed genes are detected, as described below, by  
20 comparing the pattern of gene expression between the experimental and control conditions.

Once a particular gene has been identified through the use of one such experiment, its expression pattern may be further characterized by studying its expression in a  
25 different experiment and the findings may be validated by an independent technique. Such use of multiple experiments may be useful in distinguishing the roles and relative importance of particular genes in breast cancer and the treatment thereof. A combined approach, comparing gene expression pattern in cells derived from breast cancer patients to those of *in vitro* cell culture models can give substantial hints on  
30 the pathways involved in development and/or progression of breast cancer. It can

also elucidate the role of such genes in the development of resistance or insensitivity to certain therapeutic agents (e.g. chemotherapeutic drugs).

5 Among the experiments which may be utilized for the identification of differentially expressed genes involved in malignant neoplasia and breast cancer in particular, are experiments designed to analyze those genes which are involved in signal transduction. Such experiments may serve to identify genes involved in the proliferation of cells.

10 Below are methods described for the identification of genes which are involved in breast cancer. Such represent genes which are differentially expressed in breast cancer conditions relative to their expression in normal, or non-breast cancer conditions or upon experimental manipulation based on clinical observations. Such differentially expressed genes represent "target" and/or "marker" genes. Methods for  
15 the further characterization of such differentially expressed genes, and for their identification as target and/or marker genes, are presented below.

Alternatively, a differentially expressed gene may have its expression modulated, i.e., quantitatively increased or decreased, in normal versus breast cancer states, or under  
20 control versus experimental conditions. The degree to which expression differs in normal versus breast cancer or control versus experimental states need only be large enough to be visualized via standard characterization techniques, such as, for example, the differential display technique described below. Other such standard characterization techniques by which expression differences may be visualized  
25 include but are not limited to quantitative RT-PCR and Northern analyses, which are well known to those of skill in the art.

In Addition to the experiments described above the following describes algorithms and statistical analyses which can be utilized for data evaluation and for the  
30 classification as well as response prediction for a sofar not classsified biological

sample in the context of control samples. Predictive algorithms and equations described below have already shown their power to subdivide individual cancers.

**EXAMPLE 1****Expression profiling utilizing quantitative kinetic RT-PCR**

5 For a detailed analysis of gene expression by quantitative PCR methods, one will utilize primers flanking the genomic region of interest and a fluorescent labeled probe hybridizing in-between. Using the PRISM 7700 Sequence Detection System of PE Applied Biosystems (Perkin Elmer, Foster City, CA, USA) with the technique of a fluorogenic probe, consisting of an oligonucleotide labeled with both a fluorescent  
10 reporter dye and a quencher dye, one can perform such a expression measurement. Amplification of the probe-specific product causes cleavage of the probe, generating an increase in reporter fluorescence. Primers and probes were selected using the Primer Express software and localized mostly in the 3' region of the coding sequence or in the 3' untranslated region (see Table 5 for primer- and probe- sequences). All  
15 primer pairs were checked for specificity by conventional PCR reactions and gel electrophoresis. To standardize the amount of sample RNA, GAPDH was selected as a reference, since it was not differentially regulated in the samples analyzed. To performe such an expression analysis of genes within a biological samples the respective primer/probes are prepared by mixing 25 µl of the 100 µM stock solution  
20 "Upper Primer", 25 µl of the 100 µM stock solution "Lower Primer" with 12,5 µl of the 100 µM stock solution TaqMan-probe (FAM/Tamra) and adjusted to 500 µl with aqua dest ( Primer/probe-mix). For each reaction 1,25 µl cDNA of the patient samples were mixed with 8,75 µl nuclease-free water and added to one well of a 96 Well-Optical Reaction Plate (Applied Biosystems Part No. 4306737). 1,5 µl of the  
25 Primer/Probe-mix described above, 12,5µl Taq Man Universal-PCR-mix (2x) (Applied Biosystems Part No. 4318157) and 1 µl Water are then added. The 96 well plates are closed with 8 Caps/Strips (Applied Biosystems Part Number 4323032) and centrifuged for 3 minutes. Measurements of the PCR reaction are done according to the instructions of the manufacturer with a TaqMan 7900 HT from Applied  
30 Biosystems (No. 20114) under appropriate conditions (2 min. 50°C, 10 min. 95°C, 0.15 min. 95°C, 1. min. 60°C; 40 cycles). Prior to the maesurement of so far

unclassified biological samples control experiments will e.g. cell lines, healthy control samples, samples of defined therapy response could be used for standardization of the experimental conditions.

5 TaqMan validation experiments were performed showing that the efficiencies of the target and the control amplifications are approximately equal which is a prerequisite for the relative quantification of gene expression by the comparative  $\Delta\Delta C_T$  method, known to those with skills in the art. Herefor the SoftwareSDS 2.0 from Applied Biosystems can be used according to the respective instructions. CT-values are then  
10 further analyzed with appropriate software (Microsoft Excel<sup>TM</sup>) of statistical software packages (SAS).

As well as the technology described above, provided by Perkin Elmer, one may use other technique implementations like Lightcycler<sup>TM</sup> from Roche Inc. or iCycler from  
15 Stratagene Inc. capable of real time detection of an RT-PCR reaction.

## EXAMPLE 2

### Expression profiling utilizing DNA microarrays

20 Expression profiling can be carried out using the Affymetrix Array Technology. By hybridization of mRNA to such a DNA-array or DNA-Chip, it is possible to identify the expression value of each transcripts due to signal intensity at certain position of the array. Usually these DNA-arrays are produced by spotting of cDNA,  
25 oligonucleotides or subcloned DNA fragments. In case of Affymetrix technology app. 400.000 individual oligonucleotide sequences were synthesized on the surface of a silicon wafer at distinct positions. The minimal length of oligomers is 12 nucleotides, preferable 25 nucleotides or full length of the questioned transcript. Expression profiling may also be carried out by hybridization to nylon or nitro-  
30 cellulose membrane bound DNA or oligonucleotides. Detection of signals derived from hybridization may be obtained by either colorimetric, fluorescent, electro-

chemical, electronic, optic or by radioactive readout. Detailed description of array construction have been mentioned above and in other patents cited. To determine the quantitative and qualitative changes in the chromosomal region to analyze, RNA from tumor tissue which is suspected to contain such genomic alterations has to be compared to RNA extracted from benign tissue (e.g. epithelial breast tissue, or micro dissected ductal tissue) on the basis of expression profiles for the whole transcriptome. With minor modifications, the sample preparation protocol followed the Affymetrix GeneChip Expression Analysis Manual (Santa Clara, CA). Total RNA extraction and isolation from tumor or benign tissues, biopsies, cell isolates or cell containing body fluids can be performed by using TRIzol (Life Technologies, Rockville, MD) and Oligotex mRNA Midi kit (Qiagen, Hilden, Germany), and an ethanol precipitation step should be carried out to bring the concentration to 1 mg/ml. Using 5–10 mg of mRNA to create double stranded cDNA by the SuperScript system (Life Technologies). First strand cDNA synthesis was primed with a T7-(dT24) oligonucleotide. The cDNA can be extracted with phenol/chloroform and precipitated with ethanol to a final concentration of 1mg /ml. From the generated cDNA, cRNA can be synthesized using Enzo's (Enzo Diagnostics Inc., Farmingdale, NY) *in vitro* Transcription Kit. Within the same step the cRNA can be labeled with biotin nucleotides Bio-11-CTP and Bio-16-UTP (Enzo Diagnostics Inc., Farmingdale, NY) . After labeling and cleanup (Qiagen, Hilden (Germany) the cRNA then should be fragmented in an appropriated fragmentation buffer (e.g., 40 mM Tris-Acetate, pH 8.1, 100 mM KOAc, 30 mM MgOAc, for 35 minutes at 94 °C). As per the Affymetrix protocol, fragmented cRNA should be hybridized on the HG\_U133 arrays A and B, comprising app. 40.000 probed transcripts each, for 24 hours at 60 rpm in a 45 °C hybridization oven. After Hybridization step the chip surfaces have to be washed and stained with streptavidin phycoerythrin (SAPE; Molecular Probes, Eugene, OR) in Affymetrix fluidics stations. To amplify staining, a second labeling step can be introduced, which is recommended but not compulsive. Here one should add SAPE solution twice with an antistreptavidin biotinylated antibody. Hybridization to the probe arrays may be detected by fluorometric

scanning (Hewlett Packard Gene Array Scanner; Hewlett Packard Corporation, Palo Alto, CA).

5 After hybridization and scanning, the microarray images can be analyzed for quality control, looking for major chip defects or abnormalities in hybridization signal. Therefor either Affymetrix GeneChip MAS 5.0 Software or other microarray image analysis software can be utilized. Primary data analysis should be carried out by software provided by the manufacturer.

10 In case of the genes analyses in one embodiment of this invention the primary data have been analyzed by further bioinformatic tools and additional filter criteria. The bioinformatic analysis is described in detail below.

EXAMPLE 3

15

Data analysis from expression profiling experiments

20 According to Affymetrix measurement technique (Affymetrix GeneChip Expression Analysis Manual, Santa Clara, CA) a single gene expression measurement on one chip yields the average difference value and the absolute call. Each chip contains 16-20 oligonucleotide probe pairs per gene or cDNA clone. These probe pairs include perfectly matched sets and mismatched sets, both of which are necessary for the calculation of the average difference, or expression value, a measure of the intensity difference for each probe pair, calculated by subtracting the intensity of the mismatch from the intensity of the perfect match. This takes into consideration  
25 variability in hybridization among probe pairs and other hybridization artifacts that could affect the fluorescence intensities. The average difference is a numeric value supposed to represent the expression value of that gene. The absolute call can take the values 'A' (absent), 'M' (marginal), or 'P' (present) and denotes the quality of a  
30 single hybridization. We used both the quantitative information given by the average difference and the qualitative information given by the absolute call to identify the

genes which are differentially expressed in biological samples from individuals with breast cancer versus biological samples from the normal population. With other algorithms than the Affymetrix one we have obtained different numerical values representing the same expression values and expression differences upon comparison.

The differential expression  $E$  in one of the breast cancer groups compared to the normal population is calculated as follows. Given  $n$  average difference values  $d_1, d_2, \dots, d_n$  in the breast cancer population and  $m$  average difference values  $c_1, c_2, \dots, c_m$  in the population of normal individuals, it is computed by the equation:

$$E \equiv \exp\left(\frac{1}{m} \sum_{i=1}^m \ln(c_i) - \frac{1}{n} \sum_{i=1}^n \ln(d_i)\right) \text{ (equation 1)}$$

If  $d_j < 50$  or  $c_i < 50$  for one or more values of  $i$  and  $j$ , these particular values  $c_i$  and/or  $d_j$  are set to an “artificial” expression value of 50. These particular computation of  $E$  allows for a correct comparison to TaqMan results.

A gene is called up-regulated in breast cancer versus normal if  $E \geq$  minimal change factor given in Table 3 and if the number of absolute calls equal to ‘P’ in the breast cancer population is greater than  $n/2$ . The minimal fold change factors in Table 3 are given for those patient populations responding to a given chemotherapy (CR), non responding to a administered chemotherapy (NC) or those tissues without any pathological signs of a tumor (NB). Fold changes greater than 1 refers to an increase in gene expression in the first names tissue sample compared to the second. This regulation factors are mean values and may differ individually, here the combined profiles of all 165 genes listed in Table 1 in a cluster analysis or a principle component analysis will indicate the classification group for such sample.

According to the above, a gene is called down-regulated in breast cancer versus normal if  $E \leq$  minimal change factor given in Table 3 and if the number of absolute



calls equal to 'P' in the breast cancer population is greater than  $n/2$ . Values smaller than 1 describe an decreased expression of the given gene.

The minimal fold change factors given in Table 3 indicate also the relative up- and down-regulation of those gene indicative of tumor presence. These genes do show in the comparison of any tumor tissue to the normal healthy counterpart (NT) the highest increase or decrease factors (e.g. SEQ ID: 43, 55, 65, or 162)

The final list of differentially regulated genes consists of all up-regulated and all down-regulated genes in biological samples from individuals with breast cancer versus biological samples from the normal population or of an individual response pattern. Those genes on this list which are interesting for a diagnostic or pharmaceutical application were finally validated by quantitative real time RT-PCR (see Example 1). If a good correlation between the expression values/behavior of a transcript could be observed with both techniques, such a gene is listed in Tables 1 to 5.

**Table 1:** List of 165 genes which are differentially expressed in responders compared to non-responders or normal healthy tissue. Reference is given to the SEQ ID NOs of the sequence listing.

SEQ ID NO: (DNA Sequence)	SEQ ID NO: (Protein Sequence)	Gene_Symbol	Ref. Sequences [A]	Gene_ID	Locus_Link _ID
1	166	CTSB	NM_001908	4503138	1508
2	167	SSR1	NM_003144	14781630	6745
3	168	STX8	NM_002803	4506208	5701
4	169	KPNA2	NM_002266	4504896	3838
5	170	CSE1L	NM_001316	18591914	1434
6	171	RHEB2	NM_005614	18600748	6009
7	172	DKC1	NM_001363	15011921	1736
8	173	IGFBP4	NM_001552	10835020	3487
9	174	SMC1L1	NM_006306	-	8243
10	175	PWP1	NM_007062	5902033	11137

SEQ ID NO: (DNA Sequence)	SEQ ID NO: (Protein Sequence)	Gene_Symbol	Ref. Sequences [A]	Gene_ID	Locus_Link _ID
11	176	HDAC2	NM_001527	4557640	3066
12	177	PRKAB1	NM_006253	18602783	5564
13	178	IMPDH2	NM_000884	4504688	3615
14	179	UBE2A	NM_003336	4507768	7319
15	180	YR-29	NM_014886	7662676	10412
16	181	MUF1	NM_006369	5453747	10489
17	182	MYO10	NM_012334	11037056	4651
18	183	EGFR	NM_005228	4885198	1956
19	184	IFRD1	NM_001550	4504606	3475
20	185	CD2BP2	NM_006110	5174408	10421
21	186	ARL3	NM_004311	4757773	403
22	187	CCNB2	NM_004701	10938017	9133
23	188	FMOD	NM_002023	18548671	2331
24	189	SLC7A8	NM_012244	14751202	23428
25	190	E2-EPF	NM_014501	7657045	27338
26	191	AGT	NM_000029	4557286	183
27	192	FHL2	NM_001450	4503722	2274
28	193	LDLC	NM_007357	6678675	22796
29	194	MGC16824	NM_020314	10092674	57020
30	195	UGDH	NM_003359	4507812	7358
31	196	MAD2L1	NM_002358	6466452	4085
32	197	DDB2	NM_000107	4557514	1643
33	198	OS4	NM_005730	5031964	10106
34	199	BCL2	NM_000633	13646672	596
35	200	SEMA3C	NM_006379	5454047	10512
36	201	DTR	NM_001945	4503412	1839
37	202	GARP	NM_005512	5031706	2615
38	203	ACK1	NM_005781	8922074	10188
39	204	EDG2	NM_001401	16950637	1902
40	205	RARRES3	NM_004585	8051633	5920
41	206	CCNH	NM_001239	17738313	902
42	207	PREP	NM_002726	4506042	5550
43	208	COL11A1	NM_001854	18548530	1301
44	209	GALC	NM_000153	4557612	2581

SEQ ID NO: (DNA Sequence)	SEQ ID NO: (Protein Sequence)	Gene_Symbol	Ref. Sequences [A]	Gene_ID	Locus_Link_ID
45	210	HMGCS2	NM_005518	5031750	3158
46	211	ZNF274	NM_016324	7706506	10782
47	212	TFF1	NM_003225	4507450	7031
48	213	RAD51	NM_002875	4506388	5888
49	214	ASNS	NM_001673	4502258	440
50	215	PCMT1	NM_005389	4885538	5110
51	216	ESR1	NM_000125	4503602	2099
52	217	ACAT1	NM_000019	4557236	38
53	218	XPA	NM_000380	4507936	7507
54	219	LAF4	NM_002285	4504938	3899
55	220	COL10A1	NM_000493	18105031	1300
56	221	KIAA1041	NM_014947	15299048	22887
57	222	PLA2G7	NM_005084	4826883	7941
58	223	GRP	NM_002091	4504158	2922
59	224	CYP2B6	NM_000767	14550410	1555
60	225	CHAD	NM_001267	4502798	1101
61	226	GALNT10	NM_017540	9055207	55568
62	227	GADD45B	NM_015675	9945331	4616
63	228	WBSCR20	NM_017528	8923713	114049
64	229	BTBD2	NM_017797	8923361	55643
65	230	PGR	NM_000926	4505766	5241
66	231	TBPL1	NM_004865	4759233	9519
67	232	C4B	NM_000592	14577918	721
68	233	CCNG1	NM_004060	-	900
69	234	PDHB	NM_000925	4505686	5162
70	235	HNRPDL	NM_005463	14110410	9987
71	236	TAF11	NM_005643	5032150	6882
72	237	AMACR	NM_014324	14725899	23600
73	238	EMD	NM_000117	4557552	2010
74	239	NR2F1	NM_005654	5032172	7025
75	240	HSF2	NM_004506	6806888	3298
76	241	SPG4	NM_014946	-	6683
77	242	TRIP11	NM_004239	10863904	9321
78	243	OCLN	NM_002538	9257230	4950

SEQ ID NO: (DNA Sequence)	SEQ ID NO: (Protein Sequence)	Gene_Symbol	Ref. Sequences [A]	Gene_ID	Locus_Link _ID
79	244	CACNA1D	NM_000720	-	776
80	245	CYP2B7	NR_001278	14550410	1556
81	246	FHL1	NM_001449	4503720	2273
82	247	MSX2	NM_002449	18560141	4488
83	248	PAI-RBP1	NM_015640	7661625	26135
84	249	CLDN14	NM_012130	18593128	23562
85	250	ITPK1	NM_014216	18583687	3705
86	251	ERBB2	NM_004448	4758297	2064
87	252	TP53	NM_000546	8400737	7157
88	253	HSPA2	NM_021979	13676856	3306
89	254	LIG1	NM_015541	18554950	26018
90	255	GSS	NM_000178	4504168	2937
91	256	PRO1843	NM_018507	8924082	55378
92	257	MKI67	NM_002417	4505188	4288
93	258	BIK	NM_001197	7262371	638
94	259	KIAA0225	D86978	18566873	23165
95	260	TNRC15	AB014542	18550089	26058
96	261	SFRS5	NM_006925	5902077	6430
97	262	RPL17	NM_000985	14591906	6139
98	263	GNG12	NM_018841	-	55970
99	264	LAP1B	NM_015602	17488747	26092
100	265	LOC253782	AL080192	-	253782
101	266	COL5A1	NM_000093	18571690	1289
102	267	CXCL13	NM_006419	5453576	10563
103	268	TTS-2.2	AF055000	3231586CB1	57104
104	269	KIAA0056	D29954	18578675	23310
105	270	FLJ22642	AI700633	-	-
106	271	LOC113146	W28438	15300131	113146
107	272	GPR126	NM_020455	18562351	57211
108	273	PMSCL1	NM_005033	4826921	5393
109	274	KIAA0418	NM_014631	7662103	-
110	275	SULF1	NM_015170	18571189	23213
111	276	KIAA0673	NM_015102	14720169	261734
112	277	FLJ10803	NM_018224	-	55744

SEQ ID NO: (DNA Sequence)	SEQ ID NO: (Protein Sequence)	Gene_Symbol	Ref. Sequences [A]	Gene_ID	Locus_Link_ID
113	278	DKFZp586M0723	AL050227	-	-
114	279	C4A	NM_007293	14577920	720
115	280	ZAP3	L40403	18597333	56252
116	281	NEK9	NM_033116	14916458	91754
117	282	FLJ13125	AK023187	14726621	-
118	283	FMO5	NM_001461	4503760	2330
119	284	COMP	NM_000095	4557482	1311
120	285	CSPG2	NM_004385	4758081	1462
121	286	LOC151996	AA418080	18554956	-
122	287	TFAP2B	NM_003221	4507442	7021
123	288	OR7E38P	AF065854	18544324	10821
124	289	RAB31	NM_006868	5803130	11031
125	290	HSPC126	NM_014166	14759175	29079
126	291	UMP-CMPK	NM_016308	7706496	51727
127	292	FLJ22195	NM_022758	12232426	64771
128	293	DCTN4	NM_016221	14733974	51164
129	294	FLJ20273	NM_019027	9506670	54502
130	295	KIF4A	NM_012310	14765683	24137
131	296	THTP	NM_024328	13236576	79178
132	297	PLSCR4	NM_020353	9966818	57088
133	298	FLJ11323	NM_018390	8922994	55344
134	299	MGC11242	NM_024320	13236560	79170
135	300	CEGP1	NM_020974	10190747	57758
136	301	SRR	NM_021947	8922495	63826
137	302	HSPC177	NM_015961	7705488	51510
138	303	MGC3103	NM_024036	13128987	78999
139	304	FLJ20641	NM_017915	8923595	55010
140	305	FLJ13646	NM_024584	13375767	79635
141	306	KCNK15	NM_022358	16507967	60598
142	307	RNASEL	NM_021133	10863928	6041
143	308	CRSP6	NM_004268	18577903	9440
144	309	COL5A2	NM_000393	16554580	1290
145	310	LOC51218	NM_016417	9994192	51218
146	311	APBB2	NM_173075	18557629	323

SEQ ID NO: (DNA Sequence)	SEQ ID NO: (Protein Sequence)	Gene_Symbol	Ref. Sequences [A]	Gene_ID	Locus_Link _ID
147	312	yy15c12.s1	N31716	-	-
148	313	AD037	NM_032023	14042936	83937
149	314	FLJ20477	AA203365	8923441	-
150	315	MARKL1	NM_031417	13899224	57787
151	316	LUM	NM_002345	4505046	4060
152	317	COL3A1	NM_000090	15149480	1281
153	318	COL1A1	NM_000088	18587373	1277
154	319	BF	NM_001710	14550403	629
155	320	ADAM12	NM_003474	13259517	8038
156	321	LOXL1	NM_005576	5031882	4016
157	322	CEACAM6	NM_002483	4505340	4680
158	323	MMP11	NM_005940	13027795	4320
159	324	MMP1	NM_002421	13027798	4312
160	325	MMP13	NM_002427	13027796	4322
161	326	SERPINH1	NM_001235	4757923	872
162	327	PITX1	NM_002653	4505824	5307
163	328	RAD52	NM_015419	18390318	25878
164	329	INHBA	NM_002192	4504698	3624
165	330	CSPG2	NM_004385	4758081	1462

**Table 2:** List of 47 preferred genes which differentially expressed in responders compared to non responders or normal healthy tissue. Listed genes are preferred genes, e.g., for use in the assessment whether or not a subject is expected to respond or not to respond to a given mode of treatment.

SEQ ID NO: (DNA Sequence)	SEQ ID NO: (Protein Sequence)	Gene Symbol	Ref. Sequences [A]	Gene_ID	Locus_Link _ID
4	169	KPNA2	NM_002266	4504896	3838
5	170	CSE1L	NM_001316	18591914	1434
6	171	RHEB2	NM_005614	18600748	6009
7	172	DKC1	NM_001363	15011921	1736
8	173	IGFBP4	NM_001552	10835020	3487
11	176	HDAC2	NM_001527	4557640	3066
12	177	PRKAB1	NM_006253	18602783	5564
13	178	IMPDH2	NM_000884	4504688	3615
15	180	YR-29	NM_014886	7662676	10412
22	187	CCNB2	NM_004701	10938017	9133
23	188	FMOD	NM_002023	18548671	2331
24	189	SLC7A8	NM_012244	14751202	23428
25	190	E2-EPF	NM_014501	7657045	27338
26	191	AGT	NM_000029	4557286	183
27	192	FHL2	NM_001450	4503722	2274
29	194	MGC16824	NM_020314	10092674	57020
31	196	MAD2L1	NM_002358	6466452	4085
32	197	DDB2	NM_000107	4557514	1643
40	205	RARRES3	NM_004585	8051633	5920
43	208	COL11A1	NM_001854	18548530	1301
50	215	PCMT1	NM_005389	4885538	5110
51	216	ESR1	NM_000125	4503602	2099
55	220	COL10A1	NM_000493	18105031	1300
58	223	GRP	NM_002091	4504158	2922
61	226	GALNT10	NM_017540	9055207	55568
65	230	PGR	NM_000926	4505766	5241
68	233	CCNG1	NM_004060	-	900

SEQ ID NO: (DNA Sequence)	SEQ ID NO: (Protein Sequence)	Gene Symbol	Ref. Sequences [A]	Gene_ID	Locus_Link _ID
69	234	PDHB	NM_000925	4505686	5162
74	239	NR2F1	NM_005654	5032172	7025
81	246	FHL1	NM_001449	4503720	2273
82	247	MSX2	NM_002449	18560141	4488
83	248	PAI-RBP1	NM_015640	7661625	26135
92	257	MKI67	NM_002417	4505188	4288
98	263	GNG12	NM_018841	-	55970
100	265	LOC253782	AL080192	-	253782
101	266	COL5A1	NM_000093	18571690	1289
104	269	KIAA0056	D29954	18578675	23310
105	270	FLJ22642	AI700633	-	-
106	271	LOC113146	W28438	15300131	113146
108	273	PMSCL1	NM_005033	4826921	5393
113	278	DKFZp586M 0723	AL050227	-	-
124	289	RAB31	NM_006868	5803130	11031
128	293	DCTN4	NM_016221	14733974	51164
132	297	PLSCR4	NM_020353	9966818	57088
129	294	FLJ20273	NM_019027	9506670	54502
133	298	FLJ11323	NM_018390	8922994	55344
138	303	MGC3103	NM_024036	13128987	78999

**Table 3:** Relative expression of 165 genes in complete responders as compared to non-responders and normal tissue. (CR - complete responder to therapy;  
NC - no change in tumor state; NT - normal healthy tissue)

5

SEQ ID NO: (DNA Sequence)	SEQ ID NO: (Protein Sequence)	Gene_Symbol	CR_vs_NC	CR_vs_NT	NC_vs_NT
1	166	CTSB	1.69033759	2.53990608	1.50260284
2	167	SSR1	1.69676002	1.56735024	0.92373125
3	168	STX8	1.42795315	1.65931125	1.16202079



SEQ ID NO: SEQ ID (DNA (Protein Sequence) Sequence)	NO: Gene_Symbol	CR_vs._NC	CR_vs_NT	NC_vs_NT
4	169 KPNA2	2.10809096	2.08540708	0.98923961
5	170 CSE1L	2.00249838	2.79008752	1.39330326
6	171 RHEB2	1.84519193	1.60184035	0.86811584
7	172 DKC1	2.25597289	2.3855889	1.0574546
8	173 IGFBP4	0.27862606	0.38691248	1.38864428
9	174 SMC1L1	1.69816116	1.71849631	1.01197481
10	175 PWP1	0.64477544	0.59496475	0.92274723
11	176 HDAC2	3.14799689	2.11008385	0.67029413
12	177 PRKAB1	0.52384682	0.56333165	1.07537477
13	178 IMPDH2	0.43342682	0.53415121	1.23239078
14	179 UBE2A	1.56667644	1.8748269	1.19669056
15	180 YR-29	0.51635771	0.3928245	0.7607604
16	181 MUF1	1.48621121	1.67042393	1.12394787
17	182 MYO10	2.64854259	1.9657171	0.74218822
18	183 EGFR	1.84523855	0.3988927	0.21617406
19	184 IFRD1	2.34518159	0.67841153	0.28927889
20	185 CD2BP2	0.40973605	0.74398402	1.81576414
21	186 ARL3	0.46877208	0.81409499	1.73665419
22	187 CCNB2	2.94729142	5.81162556	1.97185304
23	188 FMOD	0.33346407	0.24429053	0.73258426
24	189 SLC7A8	0.23327957	0.68038164	2.91659333
25	190 E2-EPF	2.50218494	4.49667635	1.79709992
26	191 AGT	0.38629467	0.52277847	1.35331525
27	192 FHL2	0.31699809	0.39190285	1.23629407
28	193 LDLC	0.56234146	0.88888889	1.58069244
29	194 MGC16824	0.51520913	0.67362665	1.30748198
30	195 UGDH	0.4487715	0.59229116	1.31980566
31	196 MAD2L1	4.48217081	6.89647789	1.53864683
32	197 DDB2	0.37904516	0.3243275	0.85564341
33	198 OS4	0.64290847	0.50896135	0.79165444
34	199 BCL2	0.37660415	0.26111358	0.69333698
35	200 SEMA3C	0.5199821	0.48877024	0.93997512
36	201 DTR	7.22480411	0.4189956	0.05799404
37	202 GARP	0.47456604	0.3525155	0.74281654

SEQ ID NO:	SEQ ID NO:	Gene_Symbol	CR_vs._NC	CR_vs_NT	NC_vs_NT
(DNA Sequence)	(Protein Sequence)				
38	203	ACK1	0.52564876	0.49278642	0.93748232
39	204	EDG2	0.71655585	0.46969319	0.6554872
40	205	RARRES3	0.24142196	1.41881212	5.87689745
41	206	CCNH	0.55809994	0.42039831	0.75326706
42	207	PREP	1.84855753	1.63361667	0.88372509
43	208	COL11A1	0.6377322	30.5047541	47.8331723
44	209	GALC	0.50650838	0.63980608	1.26316978
45	210	HMGCS2	0.04797018	0.03074921	0.64100686
46	211	ZNF274	1.70500973	0.86640362	0.50815172
47	212	TFF1	0.0321807	0.2064045	6.41392222
48	213	RAD51	3.1036169	2.89007176	0.93119475
49	214	ASNS	3.60284107	2.12910917	0.59095284
50	215	PCMT1	2.46691568	1.76150989	0.71405355
51	216	ESR1	0.12287491	0.2490413	2.02678727
52	217	ACAT1	0.51017664	0.39593742	0.7760791
53	218	XPA	0.51539825	0.52117332	1.01120505
54	219	LAF4	0.23519327	0.35275966	1.49987143
55	220	COL10A1	0.38555774	9.32859382	24.1950629
56	221	KIAA1041	1.44589009	1.01679685	0.70323246
57	222	PLA2G7	4.23491725	4.95203213	1.16933386
58	223	GRP	0.12594309	0.25636115	2.03553163
59	224	CYP2B6	0.01213194	0.12755005	10.513574
60	225	CHAD	0.02707726	0.17583189	6.49371152
61	226	GALNT10	0.32020561	0.93356021	2.91550231
62	227	GADD45B	0.51944741	0.22157381	0.42655678
63	228	WBSCR20	1.61337697	2.19652173	1.36144358
64	229	BTBD2	0.59662324	1.02610179	1.71984885
65	230	PGR	0.06700908	0.12481888	1.86271582
66	231	TBPL1	1.71529386	1.53220024	0.89325816
67	232	C4B	0.12173232	0.37926849	3.11559395
68	233	CCNG1	0.46882525	0.37588048	0.80174965
69	234	PDHB	0.48347992	0.82135629	1.69884261
70	235	HNRPD	0.62657647	0.54249869	0.86581401
71	236	TAF11	1.83477376	1.42164687	0.77483497

SEQ ID NO: SEQ ID (DNA (Protein Sequence) Sequence)	NO: Gene_Symbol	CR_vs_NC	CR_vs_NT	NC_vs_NT
72	237 AMACR	0.61312794	0.84739097	1.38207854
73	238 EMD	1.6831552	1.40144514	0.83262978
74	239 NR2F1	0.2644964	0.09725355	0.36769327
75	240 HSF2	1.72328808	1.03289666	0.5993755
76	241 SPG4	2.02820496	1.22197745	0.60249209
77	242 TRIP11	0.63637488	0.86619209	1.36113495
78	243 OCLN	0.47955471	0.70987061	1.48027033
79	244 CACNA1D	0.16768932	0.44304396	2.64205236
80	245 CYP2B7	0.01399196	0.13737489	9.81812983
81	246 FHL1	0.30932043	0.03099618	0.10020734
82	247 MSX2	0.26991798	0.51082405	1.89251586
83	248 PAI-RBP1	2.81808253	1.95566986	0.69397182
84	249 CLDN14	0.34578658	0.30319698	0.87683272
85	250 ITPK1	0.59689657	0.52128465	0.87332492
86	251 ERBB2	1.86323083	7.16756759	3.84684897
87	252 TP53	0.51575976	1.18684511	2.30115879
88	253 HSPA2	0.09735986	0.34190488	3.51176445
89	254 LIG1	0.3244685	0.36453228	1.12347509
90	255 GSS	0.58258632	0.84095907	1.44349265
91	256 PRO1843	0.57531505	0.51177072	0.88954864
92	257 MKI67	2.0943328	2.19410145	1.04763744
93	258 BIK	0.50587875	1.55537704	3.0746044
94	259 KIAA0225	2.13074615	2.13861404	1.00369255
95	260 TNRC15	0.63566173	0.69130642	1.0875382
96	261 SFRS5	0.55670226	0.25236203	0.45331597
97	262 RPL17	0.67408803	0.65848911	0.97685923
98	263 GNG12	0.39809519	0.35596632	0.89417388
99	264 LAP1B	0.59182478	0.87189088	1.47322468
100	265 LOC253782	0.33656287	1.0069827	2.99196016
101	266 COL5A1	0.48612506	1.91919073	3.94793618
102	267 CXCL13	1.09334867	2.55193586	2.33405493
103	268 TTS-2.2	0.52779839	0.24321886	0.46081774
104	269 KIAA0056	2.15880901	2.32531026	1.07712643
105	270 FLJ22642	0.50735263	0.47592636	0.93805833

SEQ ID NO:	SEQ ID NO:	Gene_Symbol	CR_vs._NC	CR_vs_NT	NC_vs_NT
(DNA Sequence)	(Protein Sequence)				
106	271	LOC113146	0.4322237	0.20955508	0.48483016
107	272	GPR126	2.97045989	1.28374752	0.4321713
108	273	PMSCL1	3.85379762	5.25959238	1.36478168
109	274	KIAA0418	0.63562548	0.58234822	0.91618138
110	275	SULF1	1.05390365	3.85641652	3.65917372
111	276	KIAA0673	0.57391504	0.57797443	1.00707314
112	277	FLJ10803	2.8794926	0.80518888	0.27962874
113	278	DKFZp586M0723	0.13647343	0.11662161	0.85453708
114	279	C4A	0.17445163	0.36240753	2.07740986
115	280	ZAP3	0.60561667	0.54605096	0.90164454
116	281	NEK9	0.42385526	0.71295236	1.6820656
117	282	FLJ13125	1.7458421	1.35110145	0.77389671
118	283	FMO5	0.08559415	0.30218827	3.53047791
119	284	COMP	0.2912537	4.73047702	16.2417748
120	285	CSPG2	0.59090269	1.88790387	3.19494885
121	286	LOC151996	0.41338598	2.34521857	5.67319337
122	287	TFAP2B	0.43320817	1.34577659	3.10653554
123	288	OR7E38P	2.4721374	2.04397969	0.82680667
124	289	RAB31	0.40394741	2.19420728	5.43191319
125	290	HSPC126	1.62954666	1.26787014	0.77805083
126	291	UMP-CMPK	1.92778452	1.24300347	0.64478341
127	292	FLJ22195	1.43061659	1.51916101	1.06189249
128	293	DCTN4	0.50788607	0.54260141	1.06835262
129	294	FLJ20273	0.38803157	0.89334309	2.30224333
130	295	KIF4A	2.22685745	3.35533346	1.50675718
131	296	THTP	0.58831486	0.8535722	1.45087649
132	297	PLSCR4	0.3444877	0.14809284	0.42989295
133	298	FLJ11323	2.11180669	1.12860006	0.53442394
134	299	MGC11242	0.39970231	0.96317642	2.40973447
135	300	CEGP1	0.06321053	0.22757341	3.6002451
136	301	SRR	0.43030252	0.50748029	1.17935701
137	302	HSPC177	0.54280584	0.75044087	1.38252174
138	303	MGC3103	2.49147139	2.67377209	1.0731699
139	304	FLJ20641	2.19559981	2.13795703	0.97374623

SEQ ID NO:	SEQ ID NO:	Gene_Symbol	CR_vs._NC	CR_vs_NT	NC_vs_NT
(DNA Sequence)	(Protein Sequence)				
140	305	FLJ13646	0.50690215	0.68417519	1.34971847
141	306	KCNK15	0.08400027	0.30393847	3.6183034
142	307	RNASEL	0.43951061	0.48409168	1.10143344
143	308	CRSP6	1.57038515	1.63575579	1.04162714
144	309	COL5A2	0.44650047	1.59810403	3.57917657
145	310	LOC51218	0.59078156	1.08711676	1.84013321
146	311	APBB2	0.34810181	0.3281072	0.94256105
147	312	yy15c12.s1	1.37222353	1.42335867	1.03726444
148	313	AD037	2.09401866	1.44748322	0.69124657
149	314	FLJ20477	0.52024352	0.42892996	0.82447919
150	315	MARKL1	1.86975496	1.64523021	0.87991755
151	316	LUM	0.81501967	1.26269875	1.54928623
152	317	COL3A1	0.60780953	1.3093042	2.15413568
153	318	COL1A1	0.55118736	1.72152105	3.1232956
154	319	BF	0.23831298	1.7123556	7.18532235
155	320	ADAM12	0.53384591	0.70372001	1.31820811
156	321	LOXL1	0.48175564	1.99702419	4.14530526
157	322	CEACAM6	0.57151883	7.72858988	13.5228963
158	323	MMP11	0.75362281	6.87206597	9.11870749
159	324	MMP1	26.1407301	117.806871	4.50664042
160	325	MMP13	0.24808412	2.09572957	8.4476569
161	326	SERPINH1	1.28483815	2.27223116	1.76849603
162	327	PITX1	1.54911156	16.9745142	10.9575802
163	328	RAD52	0.66443667	1.71706792	2.58424617
164	329	INHBA	0.72936034	4.21043511	5.77277773
165	330	CSPG2	0.77410378	1.86511138	2.40938157

Table 4

## Putative biological function of 165 marker genes

SEQ ID NO: SEQ (DNA Sequence)	ID Gene_Symbol NO: (Protein Sequence)	Gene Description
1	166	CTSB wu69b10.x1 cathepsin B
2	167	SSR1 SSR alpha subunit signal sequence receptor alpha (translocon-associated protein alpha) SSR alpha subunit signal sequence receptor, alpha (translocon-associated)
3	168	STX8 MSS1 proteasome (prosome macropain) 26S subunit ATPase 2 mammalian suppressor of sgvl; transactivation factor proteasome (prosome, macropain) 26S subunit, ATPase, 2
4	169	KPNA2 nuclear localization sequence receptor hSRP1alpha karyopherin alpha 2 (RAG cohort 1 importin alpha 1) karyopherin alpha 2 (RAG cohort 1, importin alpha 1)
5	170	CSE1L brain cellular apoptosis susceptibility protein (CSE1) brain cellular apoptosis susceptibility protein (CSE1) d chromosome segregation 1 (yeast homolog)-like CSE1 chromosome segregation 1-like (yeast)
6	171	RHEB2 D78132 ras-related GTP-binding protein Ras homolog enriched in brain 2 Rheb; ras-related GTP-binding protein Ras homologue enriched in brain; similar to rat Rheb gene ras-related GTP-binding protein
7	172	DKC1 Cbf5p homolog (CBF5) dyskeratosis congenita 1 dyskerin nucleolar protein; similar to yeast Cbf5p Cbf5p homolog
8	173	IGFBP4 df29g03.y1 insulin-like growth factor-binding protein 4 insulin-like growth factor binding protein 4
9	174	SMC1L1 KIAA0178 gene SMC1 (structural maintenance of chromosomes 1 yeast)-like 1 KIAA0178 similar to mitosis-specific chromosome segregation protein SMC1 of S.cerevisiae. SMC1 structural maintenance of chromosomes 1-like 1 (yeast)
10	175	PWP1 IEF SSP 9502 nuclear phosphoprotein similar to S. cerevisiae PWP1
11	176	HDAC2 transcriptional regulator homolog RPD3 histone deacetylase 2 similar to yeast RPD3, encoded by GenBank Accession Number X78454 transcriptional regulator homolog RPD3

SEQ ID NO: SEQ (DNA Sequence)	SEQ NO: (Protein Sequence)	ID Gene_Symbol	Gene Description
12	177	PRKAB1	5-AMP-activated protein kinase beta-1 protein kinase AMP-activated beta 1 non-catalytic subunit protein kinase, AMP-activated, beta 1 non-catalytic subunit
13	178	IMPDH2	(clone FFE-7) type II inosine monophosphate dehydrogenase (IMPDH2) gene exons 1-13 IMP (inosine monophosphate) dehydrogenase 2 NAD-dependent; differentiation; inosine monophosphate dehydrogenase; inosine-5'-monophosphate dehydrogenase; nucleotide biosynthesis; proliferation associated gene IMP (inosine monophosphate) dehydrogenase 2
14	179	UBE2A	HUM-HR6A HHR6A (yeast RAD 6 homologue) ubiquitin-conjugating enzyme E2A (RAD6 homolog)
15	180	YR-29	hypothetical protein clone YR-29 hypothetical protein
16	181	MUF1	MUF1 protein MUF1 protein
17	182	MYO10	KIAA0799 protein myosin X hg01449 cDNA clone for KIAA0799 has a 1204-bp insertion at position 373 of the sequence of KIAA0799. KIAA0799 protein
18	183	EGFR	HSEGFPRE precursor of epidermal growth factor receptor epidermal growth factor receptor (avian erythroblastic leukemia viral (v-erb-b) oncogene homolog) epidermal growth factor receptor; signal peptide epidermal growth factor receptor epidermal growth factor receptor (erythroblastic leukemia
19	184	IFRD1	BAC clone RG163K11 from 7q31 interferon-related developmental regulator 1 nucleophosmin 1 (nucleolar phosphoprotein B23 numatrin) pseudogene 14 HTG similar to mouse interferon-related protein PC4; 96% identical to P19182 (PID:g135861); H_RG163K11.1
20	185	CD2BP2	zk74b08.r1 CD2 antigen (cytoplasmic tail)-binding protein 2 CD2 antigen (cytoplasmic tail) binding protein 2
21	186	ARL3	48c8 ADP-ribosylation factor-like 3 EST
22	187	CCNB2	DKFZp434B174 (from clone DKFZp434B174) cyclin B2 cyclins B2 hypothetical protein
23	188	FMOD	fibromodulin fibromodulin precursor fibromodulin Encodes only the most carboxy terminal 58 amino acids of fibromodulin. fibromodulin

SEQ ID NO: SEQ (DNA Sequence)	SEQ NO:	ID Gene_Symbol	Gene Description
24	189	SLC7A8	SLC7A8 protein solute carrier family 7 (cationic amino acid transporter y <sup>+</sup> system) member 8 solute carrier family 7 (cationic amino acid transporter,
25	190	E2-EPF	HUME2EPI ubiquitin carrier protein (E2-EPF) ubiquitin carrier protein
26	191	AGT	G angiotensinogen serine (or cysteine) proteinase inhibitor clade A (alpha-1 antiproteinase antitrypsin) member 8 angiotensinogen (serine (or cysteine) proteinase inhibitor,
27	192	FHL2	heart protein (FHL-2) four and a half LIM domains 2
28	193	LDLC	LDLC low density lipoprotein receptor defect C complementing
29	194	MGC16824	hypothetical protein
30	195	UGDH	UDP-glucose dehydrogenase (UGDH) UDP-glucose dehydrogenase UDPGDH; NAD <sup>+</sup> -linked oxidoreductase
31	196	MAD2L1	UDP-glucose dehydrogenase
32	197	DDB2	MAD2 protein MAD2 (mitotic arrest deficient yeast homolog)-like 1 MAD2 gene MAD2-like 1 MAD2 mitotic arrest deficient-like 1 (yeast)
33	198	OS4	HSU18300 damage-specific DNA binding protein p48 subunit (DDB2) damage-specific DNA binding protein 2 (48kD) damage-specific DNA binding protein p48 subunit; implicated in Xeroderma pigmentosum group E DDBb p48
34	199	BCL2	OS-4 protein (OS-4) conserved gene amplified in osteosarcoma
35	200	SEMA3C	HUMBCL2A B-cell leukemia lymphoma 2 (bcl-2) proto-oncogene encoding bcl-2-alpha protein B-cell leukemialymphoma 2 (bcl-2) proto-oncogene encoding bcl-2-alpha protein B-cell lymphoma protein 2 beta splicing; bcl-2-alpha protein; proto-oncogene bcl2-alpha protein B-cell lymphoma protein 2 beta
			AB000220 semaphorin E sema domain immunoglobulin domain (Ig) short basic domain secreted (semaphorin) 3C semaphorin E sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3C



SEQ ID NO: SEQ (DNA Sequence)	SEQ NO: (Protein Sequence)	ID Gene_Symbol	Gene Description
36	201	DTR	heparin-binding EGF-like growth factor diphtheria toxin receptor (heparin-binding epidermal growth factor-like growth factor) heparin-binding EGF-like growth factor putative diphtheria toxin receptor (heparin-binding epidermal growth factor-like growth factor)
37	202	GARP	garp gene glycoprotein A repetitions predominantprecursor glycoprotein A repetitions predominant GARP gene; leucine-rich repeat containing protein glycoprotein A repetitions predominant precursor
38	203	ACK1	HUMNRTYKIN activated p21cdc42Hs kinase (ack) activated p21cdc42Hs kinase putative activated p21cdc42Hs kinase
39	204	EDG2	wc44d05.x1 endothelial differentiation lysophosphatidic acid G-protein-coupled receptor 2 EST
40	205	RARRES3	retinoic acid receptor responder 3 (RARRES3) retinoic acid receptor responder (tazarotene induced) 3 putative class II tumor suppressor; growth inhibitory protein; tazarotene induced retinoic acid receptor responder 3
41	206	CCNH	HSU11791 cyclin H cyclin H
42	207	PREP	prolyl oligopeptidase prolyl endopeptidase prolyl oligopeptidase prolyl endopeptidase
43	208	COL11A1	alpha-1 type XI collagen (COL11A1) collagen type XI alpha 1 alpha-1 type XI collagen; collagen; type XI collagen
44	209	GALC	alpha-1 (type XI) collagen precursor collagen, type XI, alpha 1
45	210	HMGCS2	DNAgalactocerebrosidase galactosylceramidase (Krabbe disease) GALC galactocerebrosidase
			3-hydroxy-3-methylglutaryl coenzyme A synthase 3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial) hydroxymethyl-CoA synthetase 3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial)
46	211	ZNF274	zinc finger protein zfp2 (zf2) KRAB zinc finger protein HFB101L zinc finger protein 274
47	212	TFF1	EST186646 trefoil factor 1 (breast cancer estrogen-inducible sequence expressed in) EST trefoil factor 1 (breast cancer, estrogen-inducible sequence
48	213	RAD51	DKFZp564H1178_s1 RAD51 (S. cerevisiae) homolog (E coli RecA homolog) EST RAD51 homolog (RecA homolog, E. coli) (S. cerevisiae)

SEQ ID NO: SEQ (DNA Sequence)	NO: (Protein Sequence)	ID Gene_Symbol	Gene Description
49	214	ASNS	asparagine synthetase asparagine synthetase asparagine synthetase
50	215	PCMT1	carboxyl methyltransferase protein-L-isoaspartate (D-aspartate) O-methyltransferase carboxyl methyltransferase protein-L-isoaspartate (D-aspartate) O-methyltransferase
51	216	ESR1	HSERR oestrogen receptor estrogen receptor 1 estrogen receptor; receptor; steroid hormone receptor oestrogen receptor
52	217	ACAT1	MAT genemitochondrial acetoacetyl-CoA thiolase acetyl-Coenzyme A acetyltransferase 1 (acetoacetyl Coenzyme A thiolase) (ACAT1) nuclear gene encoding mitochondrial prote
53	218	XPA	HUMXPAC XPAC protein xeroderma pigmentosum complementation group A XPAC protein xeroderma pigmentosum, complementation group A
54	219	LAF4	lymphoid nuclear protein (LAF-4) lymphoid nuclear protein related to AF4
55	220	COL10A1	COL10A1 genecollagen (alpha-1 type X) collagen type X alpha 1 (Schmid metaphyseal chondrodysplasia) collagen, type X, alpha 1(Schmid metaphyseal chondrodysplasia)
56	221	KIAA1041	KIAA1041 protein KIAA1041 protein KIAA1041 protein
57	222	PLA2G7	LDL-phospholipase A2 phospholipase A2 group VII (platelet-activating factor acetylhydrolase plasma) PAF-acetylhydrolase phospholipase A2, group VII (platelet-activating factor acetylhydrolase, plasma)
58	223	GRP	HUMGRP5E gastrin-releasing peptide gastrin-releasing peptide gastrin-releasing peptide pre-progastrin releasing peptide gastrin-releasing peptide
59	224	CYP2B6	HUMCYP2BB cytochrome P450-IIB (hIIB1) cytochrome P450 subfamily IIB (phenobarbital-inducible) polypeptide 6 cytochrome P450 subfamily IIB (phenobarbital-inducible) cytochrome P450; cytochrome P450 IIB cytochrome P450-IIB cytochrome P450, subfamily IIB (phenobarbital-inducible)
60	225	CHAD	chondroadherin gene 5flanking region and chondroadherin precursor cartilage leucine-rich repeat protein chondroadherin

SEQ ID NO:	SEQ NO:	ID Gene_Symbol	Gene Description
61	226	GALNT10	DKFZp586H0623 (from clone DKFZp586H0623) hypothetical protein DKFZp586H0623 (DKF hypothetical protein DKFZp586H0623 similarity to N-acetylglucosaminyltransferase.; The frame shift was determined manually hypothetical protein putative UDP-GalNAc:polypeptide N-acetylglucosaminyltransferase growth arrest and DNA-damage-inducible protein GADD45beta growth arrest and DNA-damage-inducible beta growth arrest and DNA-damage-inducible, beta wh80b02.x1 putative methyltransferase zd42a12.s1 BTB (POZ) domain containing 2 hypothetical protein FLJ20386 EST progesterone receptor DNA sequence from clone 73H22 on chromosome 6q23 TBP-like 1 HTG; CpG Island dJ73H22.1 (TBP-like protein)
62	227	GADD45B	
63	228	WBSCR20	
64	229	BTBD2	
65	230	PGR	
66	231	TBPL1	
67	232	C4B	
68	233	CCNG1	
69	234	PDHB	
70	235	HNRPDL	
71	236	TAF11	
72	237	AMACR	
73	238	EMD	
74	239	NR2F1	

SEQ ID NO: (DNA Sequence)	SEQ NO: (Protein Sequence)	ID Gene_Symbol	Gene Description
75	240	HSF2	HUMHSF2 heat shock factor 2 (HSF2) heat shock factor 2 (HSF2) d heat shock transcription factor 2 heat shock factor 2 HSF2
76	241	SPG4	factor 2 HSF2 KIAA1083 protein spastic paraplegia 4 (autosomal dominant spastin) KIAA1083 protein spastic paraplegia 4 (autosomal dominant; spastin)
77	242	TRIP11	Golgi-associated microtubule-binding protein (GMAP-210) thyroid hormone receptor interactor 11 GMAP-210 gene; Golgi-associated microtubule-binding protein Golgi-associated microtubule-binding protein
78	243	OCLN	wr26e08.x1 tight junction protein occludin d occludin EST
79	244	CACNA1D	wf59c07.x1 calcium channel voltage-dependent L type alpha 1D subunit ESTs calcium channel, voltage-dependent, L type, alpha 1D
80	245	CYP2B7	cytochrome P450-IIB (hIIB3) ds cytochrome P450, subfamily IIB (phenobarbital-inducible),
81	246	FHL1	LIM protein SLIMMER LIM protein SLIMMER d four and a half LIM domains 1 skeletal and cardiac muscle SLIM isoform LIM protein SLIMMER
82	247	MSX2	MSX-2 msh (Drosophila) homeo box homolog 2 msh homeo box homolog 2 (Drosophila)
83	248	PAI-RBP1	DKFZp564M2423 (from clone DKFZp564M2423) Similar to DKFZP564M2423 protein clone MGC:13 DKFZP564M2423 protein
84	249	CLDN14	CLDN14 gene claudin 14 (CLDN14) d claudin 14 claudin-14; CLDN14 gene claudin-14
85	250	ITPK1	inositol 1 3 4-trisphosphate 5 6-kinase inositol 1 3 4-trisphosphate 56-kinase d inositol 1 3 4-trisphosphate 5/6 kinase inositol 1,3,4-trisphosphate 5/6 kinase
86	251	ERBB2	tyrosine kinase-type receptor (HER2) v-erb-b2 avian erythroblastic leukemia viral oncogene homolog 2 (neuroglioblastoma derived oncogene homolog) v-erb-b2 avian erythroblastic leukemia viral oncogene homolog 2 (neuroglioblastoma derived oncogene homolog) tyrosine kinase HER2 receptor v-erb-b2 avian erythroblastic leukemia viral oncogene homolog 2 (neuroglioblastoma derived oncogene homolog)

SEQ ID NO: SEQ (DNA Sequence)	SEQ NO: (Protein Sequence)	ID Gene_Symbol	Gene Description
87	252	TP53	HSP53 p53 cellular tumor antigen p53 cellular tumor antigen d tumor protein p53 (Li-Fraumeni syndrome) antigen; tumor antigen p53 tumor antigen (aa 1-?) tumor protein p53
88	253	HSPA2	HUMHSPA2A heat shock protein HSPA2 gene heat shock protein d heat shock 70kD protein 2
89	254	LIG1	DKFZp434N0910_s1 for membrane glycoprotein LIG-1d DKFZP586O1624 protein EST
90	255	GSS	wt55b10.x1 (clone pGSH1) glutathione synthetase (gsh-s) d glutathione synthetase
91	256	PRO1843	initiation factor 4B eukaryotic translation initiation factor 4B
92	257	MKI67	HSMKI67 mki67a (long type) antigen of monoclonal antibody Ki-67 antigen identified by monoclonal antibody Ki-67
93	258	BIK	HSU34584 Bcl-2 interacting killer (BIK) BCL2-interacting killer (apoptosis-inducing) Bik (Bcl-2 interacting killer); Bcl-2 homology 3 (BH3) domain Bik interacts with the survival proteins Bcl-2, Bcl-xL, EBV-BHRF1 and adenovirus E1B 19kD; This protein is identical with that described by Robin Brown and colleagues (personal communication) which is a Human NBK apoptotic inducer protein, encoded by GenB Bik KIAA0225 gene KIAA0225 protein
94	259	KIAA0225	KIAA0225 gene KIAA0225 protein
95	260	TNRC15	KIAA0642 protein trinucleotide repeat containing 15
96	261	SFRS5	zc81g05.s1 splicing factor arginineserine-rich 5 ESTs
97	262	RPL17	L23 putative ribosomal protein ribosomal protein L17 ribosomal protein putative ribosomal protein (AA 1-184) ribosomal protein L17
98	263	GNG12	DKFZp586B0918 (from clone DKFZp586B0918) DKFZp586B0918 Zp586B0918)
99	264	LAP1B	UI-H-B10-aao-g-10-0-UI.s1 FLJ11551 fis clone HEMBA1002999 moderately similar to Rattus norvegicus lamina associated polypeptide 1C (LAP1C) mRN DKFZP586G011 protein
100	265	LOC253782	DKFZp434B102 (from clone DKFZp434B102) : FLJ21238 fis clone COL01115 Homo sapiens mRNA; cDNA
101	266	COL5A1	DKFZp434B102 (from clone DKFZp434B102) pro-alpha-1 (V) collagen collagen type V alpha 1

SEQ ID NO: (DNA Sequence)	SEQ NO: (Protein Sequence)	ID Gene_Symbol	Gene Description
102	267	CXCL13	B lymphocyte chemoattractant BLC small inducible cytokine B subfamily (Cys-X-Cys motif) member 13 (B-cell chemoattractant) small inducible cytokine B subfamily (Cys-X-Cys motif), clone 24519 unknown transport-secretion protein 2.2
103	268	TTS-2.2	
104	269	KIAA0056	KIAA0056 gene KIAA0056 protein
105	270	FLJ22642	we38g03.x1 : FLJ22642 fis clone HSI06970 EST
106	271	LOC113146	47g10 ESTs
107	272	GPR126	DNA sequence from clone 287G14 on chromosome 6q23.1-24.3. Contains a novel seven transmembrane domain protein gene and an exon similar to parts of BMP and Tollid genes. Contains ESTs an STS and GSSs DNA sequence from clone 287G14 on chromosome 6q23.1-24.3. Contains a novel seven transmembrane domain protein gene and an exon similar to parts of BMP and Tollid genes. Contains ESTs an STS and GS Human DNA sequence from clone 287G14 on chromosome 6q23.1-24.3. Contains a novel seven transmembrane domain protein gene and an exon similar to parts of BMP and Tollid genes. Contains ESTs an STS and GSSs HTG; BMP; seven transmembrane domain; Tollid supported by GENSCAN and FGENES dJ287G14.1 (exon of a yet unidentified gene, or part of a pseudogene?; similar to parts of BMP and Tollid proteins)
108	273	PMSCL1	tx67e10.x1 polymyositiscleroderma autoantigen 1 (75kD) EST Weakly similar to JH0446 75K autoantigen - human [H.sapiens]
109	274	KIAA0418	wi34b03.x1 KIAA0418 gene product EST
110	275	SULF1	KIAA1077 protein KIAA1077 protein KIAA1077 protein
111	276	KIAA0673	KIAA0673 protein for KIAA0673 proteind KIAA0673 protein KIAA0673 protein
112	277	FLJ10803	ni36d11.s1 hypothetical protein FLJ10803 ESTs
113	278	DKFZp586M07	DKFZp586M0723 (from clone DKFZp586M0723) DKFZp586M0723 Zp586M0723)

SEQ ID NO: SEQ (DNA Sequence)	NO: (Protein Sequence)	ID Gene_Symbol	Gene Description
114	279	C4A	RP1 and complement C4B precursor (C4B) genes complement component C4A d complement component 4B complement component 4A
115	280	ZAP3	(clone zap3) of cds and unknown ge ZAP3 protein ORF; putative
116	281	NEK9	Untitled hypothetical protein MGC16714
117	282	FLJ13125	FLJ13125 fis clone NT2RP3002877
118	283	FMO5	flavin-containing monooxygenase 5 (FMO5) FLJ12110 fis clone MAMMA1000020 highly similar to for flavin-containing monooxygenase 5 (FMO5) flavin containing monooxygenase 5 flavin-containing monooxygenase 5 flavin containing monooxygenase 5
119	284	COMP	germline oligomeric matrix protein (COMP) cartilage oligomeric matrix protein (pseudoachondroplasia epiphyseal dysplasia 1 multiple) cartilage oligomeric matrix protein (pseudoachondroplasia,
120	285	CSPG2	pgH3 proteoglycan PG-M(V3) chondroitin sulfate proteoglycan 2 (versican) PG-M; proteoglycan PG-M(V3); large chondroitin sulfate proteoglycan; pgH3; major extracellular matrix molecule proteoglycan PG-M(V3)
121	286	LOC151996	zv97h07.s1 FLJ12280 fis clone MAMMA1001744 EST
122	287	TFAP2B	transcription factor AP-2 beta (activating enhancer-binding protein 2 beta) transcription factor AP-2 beta (activating enhancer binding
123	288	OR7E38P	OR7E12P pseudogene complete sequence olfactory receptor family 7 subfamily E member 38 pseudogene olfactory receptor family 7 subfamily E member 12 pseudogene olfactory receptor
124	289	RAB31	low-Mr GTP-binding protein (RAB31) RAB31 member RAS oncogene family Low Mr GTP-binding protein of the Rab subfamily low-Mr GTP-binding protein Rab31 RAB31, member RAS oncogene family
125	290	HSPC126	wq62d04.x1 HSPC126 protein
126	291	UMP-CMPK	ws85a09.x1 UMP-CMP kinase EST
127	292	FLJ22195	DKFZp762L203_s1 hypothetical protein FLJ22195 Homo sapiens cDNA: FLJ22195 fis clone HRC01166
128	293	DCTN4	wz58c04.x1 dynactin p62 subunit dynactin 4 (p62)

SEQ ID NO: SEQ (DNA Sequence)	SEQ NO:	ID Gene_Symbol	Gene Description
129	294	FLJ20273	nh92d01.s1 hypothetical protein EST
130	295	KIF4A	zh97c02.s1 kinesin family member 4A EST
131	296	THTP	yi24d06.r1 hypothetical protein MGC2652 ESTs
132	297	PLSCR4	wk77f02.x1 phospholipid scramblase 4 EST
133	298	FLJ11323	ac16g07.s1 hypothetical protein FLJ11323 EST
134	299	MGC11242	zh46f04.r1 hypothetical protein MGC11242 ESTs
135	300	CEGP1	wv11f12.x1 CEGP1 protein
136	301	SRR	wq60g02.x1 serine racemase Homo sapiens cDNA FLJ13107 fis clone NT2RP3002501 weakly similar to THREONINE DEHYDRATASE CATABOLIC (EC 4.2.1.16) EST
137	302	HSPC177	wn81b08.x1 hypothetical protein CGI-34 protein hypothetical protein HSPC177
138	303	MGC3103	ws44f11.x1 hypothetical protein MGC3103 ESTs
139	304	FLJ20641	qi31h03.x1 hypothetical protein FLJ20641
140	305	FLJ13646	tg49h03.x1 hypothetical protein FLJ13646 Homo sapiens cDNA FLJ13646 fis clone PLACE1011325 EST
141	306	KCNK15	two pore potassium channel KT3.3
142	307	RNASEL	ribonuclease L (2 5-oligoadenylate synthetase-dependent) ribonuclease L (2',5'-oligoadenylate synthetase- dependent)
143	308	CRSP6	C05931 cofactor required for Sp1 transcriptional activation subunit 6 (77kD) EST cofactor required for Sp1 transcriptional activation,
144	309	COL5A2	y92e08.r1 collagen type V alpha 2 TRIAD3 protein EST
145	310	LOC51218	wf52b07.x1 clone FLB4739 EST
146	311	APBB2	DKFZp434E033 (from clone DKFZp434E033) FE65-like protein (hFE65L) Homo sapiens mRNA; cDNA DKFZp434E033 (from clone DKFZp434E033) amyloid beta (A4) precursor protein-binding, family B,
147	312	yy15c12.s1	yy15c12.s1 ESTs



SEQ ID NO: SEQ (DNA Sequence)	NO: (Protein Sequence)	ID Gene_Symbol	Gene Description
148	313	AD037	FE65-LIKE 2 AD037 protein
149	314	FLJ20477	zx56a06.r1 hypothetical protein FLJ20477 EST
150	315	MARKL1	DKFZp761B169_s1 ESTs MAP/microtubule affinity-regulating kinase like 1
151	316	LUM	lumican lumican lumican
152	317	COL3A1	pro-alpha-1 type 3 collagen collagen type III alpha 1 (Ehlers-Danlos syndrome type IV autosomal dominant)
153	318	COL1A1	COL3A1 gene; collagen; collagen alpha 1 type III; collagen type III prepro-alpha-1 type 3 collagen prepro-alpha1(I) collagen proalpha 1 (I) chain of type I procollagen (partial collagen type I alpha 1 alpha1(I)- collagen collagen, type I, alpha 1
154	319	BF	complement factor B B-factor properdin complement factor; complement factor B B-factor, properdin
155	320	ADAM12	meltrin-L precursor (ADAM12) a disintegrin and metalloproteinase domain 12 (meltrin alpha) (ADAM12) transcript variant a disintegrin and metalloproteinase domain 12 (meltrin alpha)
156	321	LOXL1	lysyl oxidase-like protein gene lysyl oxidase-like 1 lysyl oxidase-like 1
157	322	CEACAM6	non-specific crossreacting antigen carcinoembryonic antigen-related cell adhesion molecule 6 (non-specific cross reacting antigen) clone MGC:104 nonspecific cross-reacting antigen ORF1 non-specific cross reacting antigen
158	323	MMP11	stromelysin-3 matrix metalloproteinase 11 (stromelysin 3)
159	324	MMP1	skin collagenase matrix metalloproteinase 1 (interstitial collagenase)
160	325	MMP13	collagenase 3 matrix metalloproteinase 13 (collagenase 3)
161	326	SERPINH1	colligin (a collagen-binding protein) serine (or cysteine) proteinase inhibitor clade H (heat shock protein 47) member 1 collagen-binding protein; colligin colligin serine (or cysteine) proteinase inhibitor, clade H (heat
162	327	PITX1	hindlimb expressed homeobox protein backfoot (Bft) paired-like homeodomain transcription factor 1 paired-like homeodomain transcription factor 1
163	328	RAD52	DKFZp564I1922 (from clone DKFZp564I1922) adican d DKFZp564I1922 protein similarity to perlecan homolog hypothetical protein

SEQ ID NO: SEQ (DNA Sequence)	SEQ NO:	ID Gene_Symbol	Gene Description
164	329	INHBA	erythroid differentiation protein (EDF) inhibin beta A (activin A activin AB alpha polypeptide) inhibin, beta A (activin A, activin AB alpha polypeptide)
165	330	CSPG2	the chondroitin sulphate proteoglycan versican V1 splice-variant precursor peptide chondroitin sulfate proteoglycan 2 (versican)

Table 5: Primer and Probe sequences

SEQ ID NO: SEQ (DNA) (Probe)	ID SEQ NO:	ID SEQ NO:	ID Gene_Symbol	Probe	Forward Primer	Reverse Primer
4	331	332	333	KPNA2	TCTGCGCTAAGAGCCATAGGGAA	GAGCTTCTGAATTGCCAATTGTG A
5	334	335	336	CSE1L	CTGCAGCTGACAAAATTCCTGGTTACT AGGT	GCATTCTTAGAAGCGGTTCA TTGGATGCAATCAGCTTCTGA
6	448	449	450	RHEB2	ATTATCCTTCGAAAAACATCCACAGCAGT CTG	AGCTTTTGTGGAATCTTCTGCTAAA GCCCCGTCCTCAATTTTCTG
7	337	338	339	DKC1	TCTCGCTTCGGCTTCGAGTTTTTG	GCAGGTAGTTGCCGAAGCA TGGAGGAGTCTCGTCACTTTCA
8	340	341	342	IGFBP4	TCTCCATTAGGCACATTCAGTCCACT	GGTGGGAAGAAAGAATGCAA ACCCAGGAAGCCCTCATC
11	343	344	345	HDAC2	CCAAAGGAACCAATCAGAACAGCTCA	CCAAAGGAACCAATCAGAACAGCTCA GAAATTGGTGAGACTGTCAAAATTCA G
12	346	347	348	PRKAB1	AGTCGCCACAGATGTACCACTAGCCG	TTCTGTATACGCAGTCAAGTTCC CTTCGGCTGACTCACAGCAA
13	349	350	351	IMPDH2	AAGAGCTTGACCCCAAGTCCGAGCCAT	CATCATGCCAGGACATTGGT CAAACCTAAGCTCCCCCAGAGTACAT
15	352	353	354	YR-29	CAAGAAAACCCACCTAAATATGAAAGATT ATC	TGCTTTGTTGGAGATGGCTTT TTGAAACGCAAGCCCATG

SEQ ID NO:	SEQ NO:	ID SEQ NO:	ID SEQ NO:	ID Gene Symbol	Probe	Forward Primer	Reverse Primer
(DNA)	(Probe)	(Primer 1)	(Primer 2)				
22	355	356	357	CCNB2	AACTTAATAAATTCATGCCATCAAGAA	TGGCCAAGAATGTGGTGAAAG	TCAGGAGTTTGCTGCTTGA
23	358	359	360	FMOD	AGAAGATCCCCCAGTCAACACCAACC	TCCTTGAGCTAGACCTCTCTCTACAA	ACTCATTGATGCTATTGCCTTGA
24	361	362	363	SLC7A8	CATCCAACGCCGTCGCTGTGAC	TGTCTTTGCCAATGTCGCTTA	AACAGAAATGGGCATGATCCA
25	364	365	366	E2-EPF	TCGGATGCCCAGCTCAGCCG	TGGTCAACGCTGCTCAAGAG	GGCACTTGATGGTCAGCAGTAC
26	367	368	369	AGT	AAAGTGAGACCCCTCCACCCTTGTCAGGT	GCTGATCCAGCCTCACTATGC	AGATCCTTGACAGCACCAGTTG
27	370	371	372	FHL2	CATGCCATGCAGTGGCTTCAG	GTGTGCCCTGCTATGAGAAACA	CCCTCCCGTGGTGATG
29	373	374	375	MGC16824	AGCCAGGAGACGTACCTTTACCACATAG	GGGAGGACAACAGCGATGAG	CCCCGTAGAGGCTGTGCTT
31	376	377	378	MAD2L1	CACAGCTACGCTGACATTTCTGCCACTG	AAATCCGTTCACTGATCAGACAGA	CAGATCAAAATGAACAAGAACTTCC
32	379	380	381	DDB2	TCTCAGATGCACAAAAAGAAAGTGACG	TGAACATGGACGGCAAGAG	CCAATCACAGCATGGGTTGAG
40	382	383	384	RARRES3	CCAAGCGCCGTGGCCA	CAGGTGGAAAAGGCCAAGGT	AAGAGCATCCAGCAACAACCA
43	385	386	387	COL11A1	TCTATACCATCCTTATTCAAACCTTGCAT	GTGCCACCACCCCAATTTG	GTATTTCTAAATGGTACCTGTATA
50	388	389	390	PCMT1	ACAGGCAATATCAATCTTCTCCGGGCT	CCCAGGGCGTAATAGATCA	CTGCTCAACATTTGGTTCC
51	391	392	393	ESR1	ATGCCCTTTTGGCCGATGCA	GCCAAATTGTGTTTGATGGATTAA	GACAAAACCGAGTCACATCAGTAAT
55	394	395	396	COL10A1	TCCCCCTGAAAAGTGAGCAGCAACGTA	CAGATTTGAGCTATCAGACCACAA	AAATTCAGAGAGGGCTTCACATACG
58	397	398	399	GRP	CGTTCTGCAAGCATCAGTTCACG	AGAGAAAAACAAACCCCTAAGAG	GCACAAGGAAATCTTGTGATGAT
61	400	401	402	GALNT10	CCACAGCATGAAGGGCAACCAGC	ACT	TCCTGCTTTGCGGTATTCCA
65	403	404	405	PGR	TTGATAGAACCGTGTGAGCTCGA	GCCCTGTACGCTGTACGA	ACAAGATCATGCAAGTTATCAAGAA
68	406	407	408	CCNG1	ATGAAGGTACAGCCCAAGCACCTTGGG	AGCTCATCAAGGCAATTGGTTT	GTT
					GCTGTGAATTTACTGGACAGATTCC	AAATAAAGCAGCTCAGTCCAACA	

SEQ ID	SEQ NO:	ID SEQ NO:	ID SEQ NO:	ID Gene_Symbol	Probe	Forward Primer	Reverse Primer
69	409	410	411	PDHB	ATCCTGGCACAGATTTCAGCTCCTACTCC A	GAAGGAGGCTGGCCACAGT	TTGAACGCGAGGACCTTCCAT
74	412	413	414	NR2F1	TGTACAGAAATATATCCACATCCGTCACCA ATAAATCCT	TAAACAGAAAGGAAACTAATGGAC CTT	CAGTCCACTCCATATGTGTGTTC
81	415	416	417	FHL1	CACCTCACGCAATGCTTGGCA	TGCGTGACTTGCCATGAGA	GGTAAGTGATTCTCCAGATGTGA
82	418	419	420	MSX2	CAACAGCCCATTAAGTTCCCTGG	CAGAAAGGTAAAGCCCATGTTTGACT	GGGACAGATGGACAGGAAGGT
83	421	422	423	PAI-RBP1	CTGATGTGGATGACCCAGAGGCATTCC	ACCGACAAGTCAAGTGCTTCTG	GGTTGTCTTATGGCATCCAGTTAA
92	424	425	426	MKI67	TTTCTGATTCTGCATGAGAACCTTCGCA	GAGAGCGGAGGGCAGAAGA	GAGAGCGGAGGGCAGAAGA
98	427	428	429	GNG12	CCCCACCCCTCTGCTGTCCTG	CCAGATGCCCTTGTTCCAAAG	GCAGCTTATAGCACCAACACGTT
100	430	431	432	LOC253782	CCCAAAGTTTCATAAAGCCCTAAGCTCA TGA	AATGGAAAACAACCTCTGAGTTTGA	TGTGGGCAAGAGTTGATGAAA
101	433	434	435	COL5A1	CTTCGTGAGTGTCCTGCAC	CTCGTACCTCAGCATGCCATT	GTGCCGAGGCGGTAGATGAAG
104	436	437	438	KIAA0056	ACGTGCAGTCAGGTGCTTCATACA	CATCGGAGTCGGAGCTTAGG	CTCGCCATTGCGACTCTTGCT
105	439	440	441	FLJ22642	AATCTAATGTAGCAAAACGTAACCA	TGAAACGATTAGCTGTAGCCAAAT	CAGTAGATTTACCACACATATTGCA TTTT
106	442	443	444	LOC113146	AACATAGTTTCTCTATTTCAGGCAGAGTG CGGTATATTC	GGTGACAAGTCGTTTTTTGGTATAA CTTC	GCTAAGTGAGTAGGAAACAGTGTT TCC
108	445	446	447	PMSCL1	TGTTTCTACACCTGTGCTATGGACTC	TGAAGCAGAAACCTCCTTCAGAAG	TCCAATTTGGGCGAGTTCCA
113	451	452	453	DKFZp586M072 3	CAGACTAGCCCATGACTTGAATGCCAGCA	AAAGAGCGTATGAAAAGTACGTGA GACTT	TGACAAACACGACATAAATAACACA CA
124	454	455	456	RAB31	TTCCCTGAAGGATGCTAAGGAATACGC T	AACAAGTCGGACCTCTCAGATATT	AACCACGATGGCACCTATGG
128	457	458	459	DCTN4	CACCTCATCTAATATAAAAAAGGCAA	TCAATACCTGCAGCTGGTGAAT	GGTGCATACTGACTAGCATTAAAAAT TTT

SEQ ID	SEQ NO:	ID	SEQ NO:	ID	SEQ NO:	ID	Gene_Symbol	Probe	Forward Primer	Reverse Primer
(DNA)	(Probe)	(Primer 1)	(Primer 2)							
129	460	461	462	FLJ20273					GACCAATGTAATTCGGATCAGATC	GAAACTCTGTGACAATCCTTCACTA
										GA
132	463	464	465	PLSCR4					CTTGCTTCCTCATTGACTTCATGT	GGCTTGCTGTCTCTCTATCTTG
133	466	467	468	FLJ11323					GTGCTGACGGGACCCCTTCT	ACGAGAGCGAAACTCCATTG
138	469	470	471	MGC3103					GCTGGCTGACAACATGACGG	GATGGCATTGCGACACAGTGT

**EXAMPLE 4**

Analysis of differential gene expression patterns using support vector machines

5 Support vector machines (SVM) are well suited for two-class or multi-class pattern recognition (Weston and Watkins, 1999 (115); Vapnik, 1995 (116); Vapnik, 1998 (117); Burges, 1998 (118).

10 For the two-class classification problem, (e.g. tumor tissue vs. non tumor tissue, or therapy response vs. non response) assume that we have a set of samples, i.e., a series of input vectors

$$\vec{x}_i \in \mathbb{R}^d \quad (i = 1, 2, \dots, m)$$

15 with corresponding labels

$$y_i \in \{+1, -1\} \quad (i = 1, 2, \dots, m).$$

20 Here, +1 and -1 indicate the two classes. To classify gene expression patterns of marker genes from Table 1 or 2 for describing the current tumor status or probable response to a therapeutic agent, the input vector dimension is equal to the number of different oligonucleotide types present on the oligonucleotide array or a subset hereof, and each input vector unit stands for the hybridization value of one specific oligonucleotide type.

25

The goal is to construct a binary classifier or derive a decision function from the available samples which has a small probability of misclassifying a future sample.

An SVM implements the following idea: it maps the input vectors

$$\vec{x}_i \in \mathbb{R}^d$$

into a high-dimensional feature space

$$\Phi(\vec{x}) \in H$$

and constructs an Optimal Separating Hyperplane (OSH), which maximizes the margin, the distance between the hyperplane and the nearest data points of each class in the space  $H$ . By choosing OSH from among the many that can separate the positive from the negative examples in the feature space, SVMs are avoiding the risk of overfitting.

Different mappings construct different SVMs. The mapping

$$\Phi : \mathbb{R}^d \mapsto H$$

is performed by a kernel function

$$K(\vec{x}_i, \vec{x}_j)$$

which defines an inner product in the space  $H$ .

The decision function implemented by SVM can be written as (Burges, 1998 (118):

$$f(\vec{x}) = \text{sgn} \left( \sum_{i=1}^m y_i \alpha_i \cdot K(\vec{x}, \vec{x}_i) + b \right) \quad (\text{equation 2})$$

where the coefficients  $\alpha_i$  are obtained by solving the following convex Quadratic Programming (QP) problem:

$$\text{Maximize} \quad \sum_{i=1}^m \alpha_i - \frac{1}{2} \sum_{i=1}^m \sum_{j=1}^m \alpha_i \alpha_j \cdot y_i y_j \cdot K(\vec{x}_i, \vec{x}_j)$$

$$\text{subject to} \quad 0 \leq \alpha_i \leq C \quad (\text{equation 3})$$

$$5 \quad \text{and} \quad \sum_{i=1}^m \alpha_i y_i = 0$$

The regularity parameter  $C$  (equation 3) controls the trade off between margin and misclassification error. The  $\vec{x}_j$  are called Support Vectors only if the corresponding  $\alpha_i > 0$ .

10

Two of the kernel functions used in the current example:

$$K(\vec{x}_i, \vec{x}_j) = (\vec{x}_i \cdot \vec{x}_j + 1)^d \quad (\text{equation 4})$$

$$15 \quad K(\vec{x}_i, \vec{x}_j) = e^{-\gamma \|\vec{x}_i - \vec{x}_j\|^2} \quad (\text{equation 5})$$

where the first one (equation 4) is called the polynomial kernel function of degree  $d$  which will eventually revert to the linear function when  $d = 1$ , the latter (equation 5) is called the Radial Basic Function (RBF) kernel.

20

For a given data set, only the kernel function and the regularity parameter  $C$  must be selected to specify one SVM. An SVM has many attractive features. For instance, the solution of the QP problem is globally optimised while with neural networks the gradient based training algorithms only guarantee finding a local minima. In addition, SVM can handle large feature spaces, can effectively avoid overfitting (see above) by controlling the margin, can automatically identify a small subset made up of informative points, i.e., the Support Vectors, etc.

25



The classification of biological sample and thereby the identification of an neoplastic lesion as well as the response of such lesion to therapeutic agents based on gene expression data is a multi-class classification problem. The class number  $k$  is equal to the number tumor subcalsses (e.g. histological features, TNM stage, grade, hormonal status) and is equal to response subgroupe to a certain therapeutic agent (e.g. pathologically confirmed complete remission, good remission, partial remission, or no remission, as well as progressive disease) which shall be predicted, i.e., which are present in the training data set. Due to the limited number of different classes in the present sample set, we decided to handle the multi-class classification by reducing the multi-classification to a series of binary classifications. For a  $k$ -class classification,  $k$  SVMs are constructed. The  $i$ th SVM will be trained with all of the samples in the  $i$ th class with positive labels and all other samples with negative labels. Finally an unknown sample is classified into the class that corresponds to the SVM with the highest output value. This method is used to construct a prediction/classification system for gene expression patterns of differentially expressed marker genes as given in Table 1 and 2.

Each data point generated by a microarray hybridization experiment or by real time RT-PCR (cf. example 1 and 2) corresponds to and is determined by the number of mRNA copies present in the analysed sample, i.e., from an experiment with  $n$  oligonucleotide types on a polynucleotide array, a series of  $n$  expression-level values is obtained. These  $n$  values are typically stored in a metrics file which is the result of the analysis of a "cel file" by the Affymetrix® Microarray Suite or software described above. The data from a series of  $m$  metrics files (representing  $m$  expression analyses) are taken to build an expression matrix, in which each of the  $m$  rows consists of an  $n$ -element expression vector for a single experiment. In order to normalise the expression values of the  $m$  experiments, we define  $x_{ij}$  to be the sum of the logarithms of the expression level  $a_{ij}$  for gene  $j$  (whose mRNA hybridizes with the oligonucleotide type  $j'$  present on the microarray, or gives a valid  $\Delta\Delta C_T$  intensity), normalized so that the expression vector  $\vec{x}_i$  has the Euclidean length 1:

$$x_{j,i} = \frac{\ln(a_{i,j})}{\sqrt{\sum_{k=1}^n \ln(a_{i,k})^2}} \quad (\text{equation 6})$$

Initial analyses are carried out using a set of 20000-element expression vectors for  
 5 150 experiments as described in example 1 and 2 (100 experiments in the training set  
 and 50 in the test set).

Using the knowledge that the 150 experiments represent three different response  
 classes and two different tumor states as well as the information of tumor and non-  
 10 tumor tissue, we trained the SVMs described above with the training set to recognize  
 those response classes and disease states. The test set was used to assess the  
 prediction accuracy. Here we have preformed crossvalidations utilizing the “leave  
 one out” method and for more stringent testing a four to five fold validation (leave  
 25% out) with n iterations ( n>100).

15

In such crossvalidations and classification experiments the predictive power of a  
 subset of marker genes chosen from Table 1 (e.g. SEQ ID: 27, 38, 55, 81, 97, 98) has  
 been tested. The average cross validation error rate was 8.333 % with affinity levels  
 as follows:

20

Tissue sample	True response	Predicted CR	Predicted NC
Sample_1	CR	0.9141	-0.9141
Sample_2	CR	1.281	-1.281
Sample_3	CR	1.149	-1.149
Sample_4	CR	0.3987	-0.3987
Sample_5	CR	0.2182	-0.2182
Sample_6	CR	0.7127	-0.7127
Sample_7	NC	-1.124	1.124
Sample_8	NC	-1.492	1.492
Sample_9	NC	-1.896	1.896

Tissue sample	True response	Predicted CR	Predicted NC
Sample_10	NC	0.475	-0.475
Sample_11	NC	-1.962	1.962
Sample_12	NC	-0.7557	0.7557

5 The misclassification of one sample can be compensated by addition of more marker genes from Table 1. These data show the minimal number of marker genes that could be combined for a predictive assay or kit.

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06. Okt. 2003

CLAIMS

1. Method for characterizing the state of a neoplastic disease in a subject, comprising
- 5
- (i) determining the pattern of expression levels of at least 6, 7, 8, 10, 15, 20, 30, or 47 marker genes, comprised in a group of marker genes consisting of SEQ ID NO:1 to 165, in a biological sample from said subject,
- 10
- (ii) comparing the pattern of expression levels determined in (i) with one or several reference pattern(s) of expression levels,
- (iii) characterizing the state of said neoplastic disease in said subject from the outcome of the comparison in step (ii).
- 15
2. Method for detection, diagnosis, screening, monitoring, and/or prognosis of a neoplastic disease in a subject, comprising
- (i) determining the pattern of expression levels of at least 1, 2, 3, 4, 5, 10, 15, 20, 30, or 47 marker genes, comprised in a group of marker genes consisting of SEQ ID NOs:1 to 17, 19 to 33, 35 to 50, 52 to 64, 66 to 85, 88 to 91, and 93 to 165 in biological samples from said subject,
- 20
- (ii) comparing the pattern of expression levels determined in (i) with one or several reference pattern(s) of expression levels,
- (iii) detecting, diagnosing, screening, monitoring, and/or prognosing said neoplastic disease in said subject from the outcome of the comparison in step (ii).
- 25
3. Method of claim 1 or 2, wherein said method comprises multiple determinations of a pattern of expression levels, at different points in time, thereby allowing to monitor the development of said neoplastic disease in said subject.
- 30

4. Method of claim 1, wherein said method comprises an estimation of the likelihood of success of a given mode of treatment for said neoplastic disease in said subject.
- 5
5. Method of claim 1, wherein said method comprises an assessment of whether or not the subject is expected to respond to a given mode of treatment for said neoplastic disease.
- 10 6. Method of claim 4 or 5, wherein a predictive algorithm is used.
7. Method of claim 6, wherein the predictive algorithm is a Support Vector Machine.
- 15 8. Method of any of claims 4 to 7, wherein said given mode of treatment
- (i) acts on cell proliferation, and/or
  - (ii) acts on cell survival, and/or
  - (iii) acts on cell motility, and/or
  - 20 (iv) is an anthracycline based mode of treatment, and/or
  - (v) comprises administration of epirubicin and/or cyclophosphamid.
9. Method of treatment for a subject afflicted with a neoplastic disease, comprising
- 25
- (i) identifying the most promising mode of treatment with the method of claim 4 or 5,
  - (ii) treating said neoplastic disease in said patient by the mode of treatment identified in step (i).
- 30

10. Method of screening for subjects afflicted with a neoplastic disease, wherein the method of claim 1 or 2 is applied to a plurality of subjects.
- 5 11. Method of screening for substances and/or therapy modalities having curative effect on a neoplastic disease comprising
- 10 (i) obtaining a biological sample from a subject afflicted with said neoplastic disease,
- (ii) assessing, from said biological sample, using the method of claim 4 or 5, whether said subject is expected to respond to a given mode of treatment for said neoplastic disease,
- (iii) if said subject is expected to respond to said given mode of treatment, incubating said biological sample with said substance under said therapy modalities,
- 15 (iv) observing changes in said biological sample triggered by said test substance under said therapy modalities,
- (v) selecting or rejecting said test substance and/or said therapy modalities, based on the observation of changes in said biological sample under (iv).
- 20 12. Method of screening for compounds having curative effect on a neoplastic disease comprising
- 25 (i) incubating biological samples or extracts of these with a test substance,
- (ii) determining the pattern of expression levels of at least 1, 2, 3, 4, 5, 10, 15, 20, 30, or 47 marker genes, comprised in a group of marker genes consisting of SEQ ID NO:1 to 17, 19 to 33, 35 to 50, 52 to 64, 66 to 85, 88 to 91, and 93 to 165 in said biological sample,
- 30 (iii) comparing the pattern of expression levels determined in (ii) with one or several reference pattern(s),

- (iv) selecting or rejecting said test substance, based on the comparison performed under (iii).

5           13. Method of any of claims 1 to 12 wherein said marker genes are comprised in a group of marker genes listed in Table 2.

10           14. Method of any of claims 1 to 13, wherein the expression level is determined

- (i) with a hybridization based method, or
- (ii) with a hybridization based method utilizing arrayed probes, or
- (iii) with a hybridization based method utilizing individually labeled probes, or
- (iv) by real time PCR, or
- (v) by assessing the expression of polypeptides, proteins or derivatives thereof, or
- (vi) by assessing the amount of polypeptides, proteins or derivatives thereof.

15

20           15. Method of any of claims 1 to 14, wherein the neoplastic disease is breast cancer.

            16. A kit comprising at least 6, 7, 8, 10, 15, 20, 30, or 47 primer pairs and probes suitable for marker genes comprised in a group of marker genes consisting of

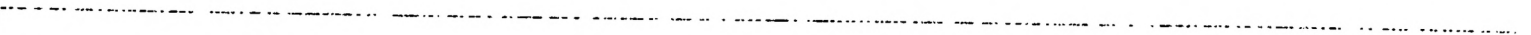
25           (i) SEQ ID NO:1 to SEQ ID NO:165, or

            (ii) the marker genes listed in Table 2.

            17. A kit comprising at least 6, 7, 8, 10, 15, 20, 30, or 47 sets of individually labeled probes, each having a sequence comprised in a group of sequences consisting of SEQ ID NO:331 to SEQ ID NO:471.

30

18. A kit comprising at least 6, 7, 8, 10, 15, 20, 30, or 47 sets of arrayed probes, each having a sequence comprised in a group of sequences consisting of SEQ ID NO:331 to SEQ ID NO:471.

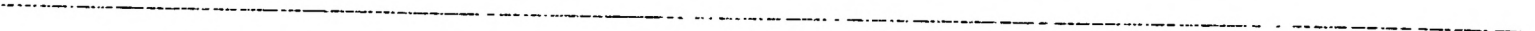


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**METHODS AND KITS FOR INVESTIGATING CANCER**

**ABSTRACT OF THE DISCLOSURE**

The invention provides novel compositions, methods and uses, for the prediction, diagnosis, prognosis, prevention and treatment of malignant neoplasia and breast cancer. The invention further relates to genes that are differentially expressed in breast tissue of breast cancer patients versus those of normal "healthy" tissue. Differentially expressed genes for the identification of patients which are likely to respond to chemotherapy are also provided.





## SEQUENCE LISTING

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&lt;211&gt; 1545

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&lt;213&gt; Homo sapiens

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&lt;210&gt; 4

&lt;211&gt; 1976

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 4

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&lt;211&gt; 3579

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 5

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&lt;210&gt; 11

&lt;211&gt; 1985

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;211&gt; 2429

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 12

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 13

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&lt;213&gt; Homo sapiens

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&lt;213&gt; Homo sapiens

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&lt;213&gt; Homo sapiens

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 19

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&lt;211&gt; 1299

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&lt;213&gt; Homo sapiens

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&lt;211&gt; 900

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 21

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;211&gt; 2863

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;213&gt; Homo sapiens

&lt;400&gt; 24

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&lt;210&gt; 25

&lt;211&gt; 890

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 25

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&lt;210&gt; 26

&lt;211&gt; 2099

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 26

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&lt;210&gt; 27

&lt;211&gt; 1892

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 27

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&lt;210&gt; 28

&lt;211&gt; 2904

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 28

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&lt;210&gt; 29

&lt;211&gt; 3611

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 29

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&lt;210&gt; 30

&lt;211&gt; 2950

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 30

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&lt;210&gt; 31

&lt;211&gt; 1390

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;210&gt; 32

&lt;211&gt; 1820

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;210&gt; 33

&lt;211&gt; 4833

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 33

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&lt;213&gt; Homo sapiens

&lt;400&gt; 34

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 36

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&lt;211&gt; 4163

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 37

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&lt;211&gt; 4548

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 38

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&lt;211&gt; 2687

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;211&gt; 768

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 40

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&lt;211&gt; 1398

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 41

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&lt;211&gt; 2756

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 42

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&lt;210&gt; 43

&lt;211&gt; 6319

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 43

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&lt;211&gt; 3986

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&lt;213&gt; Homo sapiens

&lt;400&gt; 44

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&lt;211&gt; 2058

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;211&gt; 2538

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;210&gt; 47

&lt;211&gt; 540

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 47

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&lt;210&gt; 48

&lt;211&gt; 2254

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 48

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&lt;210&gt; 49

&lt;211&gt; 1994

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 49

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&lt;210&gt; 50

&lt;211&gt; 1599

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 50

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&lt;210&gt; 51

&lt;211&gt; 6450

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 51

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&lt;210&gt; 52

&lt;211&gt; 1518

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 52

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&lt;210&gt; 53

&lt;211&gt; 1439

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 53

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&lt;210&gt; 54

&lt;211&gt; 3857

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 54

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&lt;210&gt; 55

&lt;211&gt; 3285

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 55

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&lt;211&gt; 5341

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 56

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&lt;211&gt; 1561

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 57

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&lt;213&gt; Homo sapiens

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&lt;213&gt; Homo sapiens

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;210&gt; 61

&lt;211&gt; 3164

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;211&gt; 1121

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 62

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&lt;213&gt; Homo sapiens

&lt;400&gt; 63

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&lt;211&gt; 2668

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 64

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&lt;210&gt; 65

&lt;211&gt; 5003

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 65

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&lt;210&gt; 70

&lt;211&gt; 3514

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 70

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&lt;210&gt; 71

&lt;211&gt; 1599

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 71

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&lt;211&gt; 2068

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;210&gt; 73

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&lt;213&gt; Homo sapiens

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&lt;211&gt; 1658

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

<400> 74

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<211> 2444

<212> DNA

<213> Homo sapiens

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&lt;211&gt; 3263

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 76

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&lt;210&gt; 77

&lt;211&gt; 6452

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 77

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&lt;211&gt; 2648

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;210&gt; 81

&lt;211&gt; 2398

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 81

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&lt;211&gt; 2197

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&lt;213&gt; Homo sapiens

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&lt;211&gt; 2201

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 83

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&lt;211&gt; 1233

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;210&gt; 90

&lt;211&gt; 1918

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 90

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&lt;210&gt; 91

&lt;211&gt; 1268

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 91

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&lt;210&gt; 92

&lt;211&gt; 12515

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 92

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&lt;211&gt; 848

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&lt;220&gt;

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 100

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 111

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&lt;211&gt; 1922

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;211&gt; 5417

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 114

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&lt;213&gt; Homo sapiens

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&lt;210&gt; 121

&lt;211&gt; 3187

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 121

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&lt;210&gt; 122

&lt;211&gt; 1992

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;210&gt; 123

&lt;211&gt; 942

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;211&gt; 3969

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;211&gt; 1424

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 125

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&lt;211&gt; 2836

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 126

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&lt;210&gt; 127

&lt;211&gt; 1677

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 127

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&lt;210&gt; 128

&lt;211&gt; 3837

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 128

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&lt;210&gt; 129

&lt;211&gt; 4020

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 129

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&lt;210&gt; 130

&lt;211&gt; 4348

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 130

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&lt;210&gt; 131

&lt;211&gt; 1919

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 131

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&lt;211&gt; 3206

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 132

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&lt;210&gt; 133

&lt;211&gt; 2087

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens



<400> 133

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<212> DNA

<213> Homo sapiens

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;211&gt; 2477

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 136

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&lt;211&gt; 1341

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;211&gt; 2449

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;211&gt; 6217

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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aaaaaaaaaa						4268

&lt;210&gt; 147

&lt;211&gt; 1167

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (415)..(415)

&lt;223&gt; n = a, t, g, or c

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (559)..(559)

&lt;223&gt; n = a, t, g, or c

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (602)..(602)

&lt;223&gt; n = a, t, g, or c

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (612)..(612)

&lt;223&gt; n = a, t, g, or c

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (621)..(621)

&lt;223&gt; n = a, t, g, or c

&lt;400&gt; 147

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&lt;210&gt; 148

&lt;211&gt; 2509

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 148

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&lt;210&gt; 149

&lt;211&gt; 2387

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (541)..(541)

&lt;223&gt; n = a, t, g, or c

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (706)..(706)

&lt;223&gt; n = a, t, g, or c

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (805)..(805)

&lt;223&gt; n = a, t, g, or c

&lt;400&gt; 149

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&lt;210&gt; 150

&lt;211&gt; 4917

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;211&gt; 5489

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&lt;213&gt; Homo sapiens

&lt;400&gt; 152

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&lt;213&gt; Homo sapiens

&lt;400&gt; 153

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&lt;210&gt; 154

&lt;211&gt; 2565

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 154

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&lt;211&gt; 5062

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 155

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&lt;213&gt; Homo sapiens

&lt;400&gt; 156

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&lt;211&gt; 2249

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 157

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;210&gt; 159

&lt;211&gt; 1973

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 159

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&lt;211&gt; 2722

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 160

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&lt;211&gt; 2208

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 161

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&lt;400&gt; 163

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&lt;210&gt; 164

&lt;211&gt; 1840

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 164

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gtcaccttcc	aactatccgg	tgcttaggaa	atggaagatg	ggctatacct	aaaattacct	10320
gcatgaaccc	atctgcatac	caaaggactt	attctatgaa	atactttaaa	aattcctcat	10380
cagcaaagga	caattcaata	aatacatcca	aacatgatca	tcggttgagc	cggaggtggc	10440
aggagtcgag	gcgctgatcc	ctaaaatggc	gaacatgtgt	tttcatcatt	tcagccaaag	10500
tcctaacttc	ctgtgccttt	cctatcacct	cgagaagtaa	ttatcagttg	gtttggattt	10560
ttggaccacc	gttcagtcac	tttgggttgc	cgtgctccca	aaacatttta	aatgaaagta	10620
ttggcattca	aaaagacagc	agacaaaatg	aaagaaaatg	agagcagaaa	gtaagcattt	10680
ccagcctatc	taatttcttt	agttttctat	ttgcctccag	tcagtcctat	ttcctaattg	10740
ataccagcct	actgtactat	ttaaaatgct	caatttcagc	accgatggcc	atgtaaataa	10800
gatgatttaa	tggtgatttt	aatcctgtat	ataaaaataa	aagtcacaat	gagtttgggc	10860
atatttaatg	atgattatgg	agccttagag	gtctttaatc	attgggttcg	ctgcttttat	10920
gtagtttagg	ctggaaatgg	tttcaacttc	tctttgactg	tcagcaagac	tgaagatggc	10980
ttttcctgga	cagctagaaa	acacaaaatc	ttgtaggtca	ttgcacctat	ctcagccata	11040
ggtgcagttt	gcttctacat	gatgctaaag	gctgcgaatg	ggatcctgat	ggaactaagg	11100
actccaatgt	cgaactcttc	tttgcctgat	tcctttttct	tcacttacia	gaaaggcctg	11160
aatggaggac	ttttctgtaa	ccagg				11185

**<210> 166**

**<211> 339**

**<212> PRT**

<213> Homo sapiens

**<400> 166**

[illegible]

- 231 -

&lt;210&gt; 167

&lt;211&gt; 286

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 167

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Met Arg Leu Leu Pro Arg Leu Leu Leu Leu Leu Leu Val Phe Pro
1      5      10      15
Ala Thr Val Leu Phe Arg Gly Gly Pro Arg Gly Ser Leu Ala Val Ala
20
Gln Asp Leu Thr Glu Asp Glu Glu Thr Val Glu Asp Ser Ile Ile Glu
35      40      45
Asp Glu Asp Asp Glu Ala Glu Val Glu Glu Asp Glu Pro Thr Asp Leu
50      55      60
Val Glu Asp Lys Glu Glu Asp Val Ser Gly Glu Pro Glu Ala Ser
65      70      75      80
Pro Ser Ala Asp Thr Thr Ile Leu Phe Val Lys Gly Glu Asp Phe Pro
85      90      95
Ala Asn Asn Ile Val Lys Phe Leu Val Gly Phe Thr Asn Lys Gly Thr
100      105      110
Glu Asp Phe Ile Val Glu Ser Leu Asp Ala Ser Phe Arg Tyr Pro Gln
115      120      125
Asp His Gln Phe Tyr Ile Gln Asn Phe Thr Ala Leu Pro Leu Asn Thr
130      135      140
Val Val Pro Pro Gln Arg Gln Ala Thr Phe Glu Tyr Ser Phe Ile Pro
145      150      155      160
Ala Glu Pro Met Gly Gly Arg Pro Phe Gly Leu Val Ile Asn Leu Asn
165      170      175
Tyr Lys Asp Leu Asn Gly Asn Val Phe Gln Asp Ala Val Phe Asn Gln
180      185      190
Thr Val Thr Val Ile Glu Arg Glu Asp Gly Leu Asp Gly Glu Thr Ile
195      200      205
Phe Met Tyr Met Phe Leu Ala Gly Leu Gly Leu Leu Val Ile Val Gly
210      215      220
Leu His Gln Leu Leu Glu Ser Arg Lys Arg Lys Arg Pro Ile Gln Lys
225      230      235      240
Val Glu Met Gly Thr Ser Ser Gln Asn Asp Val Asp Met Ser Trp Ile
245      250      255
Pro Gln Glu Thr Leu Asn Gln Ile Asn Lys Ala Ser Pro Arg Arg Leu
260      265      270
Pro Arg Lys Arg Ala Gln Lys Arg Ser Val Gly Ser Asp Glu
275      280      285

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&lt;210&gt; 168

&lt;211&gt; 433

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 168

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Met Pro Asp Tyr Leu Gly Ala Asp Gln Arg Lys Thr Lys Glu Asp Glu
1      5      10      15
Lys Asp Asp Lys Pro Ile Arg Ala Leu Asp Glu Gly Asp Ile Ala Leu
20      25      30

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Leu Lys Thr Tyr Gly Gln Ser Thr Tyr Ser Arg Gln Ile Lys Gln Val  
 35 40 45  
 Glu Asp Asp Ile Gln Gln Leu Leu Lys Lys Ile Asn Glu Leu Thr Gly  
 50 55 60  
 Ile Lys Glu Ser Asp Thr Gly Leu Ala Pro Pro Ala Leu Trp Asp Leu  
 65 70 75 80  
 Ala Ala Asp Lys Gln Thr Leu Gln Ser Glu Gln Pro Leu Gln Val Ala  
 85 90 95  
 Arg Cys Thr Lys Ile Ile Asn Ala Asp Ser Glu Asp Pro Lys Tyr Ile  
 100 105 110  
 Ile Asn Val Lys Gln Phe Ala Lys Phe Val Val Asp Leu Ser Asp Gln  
 115 120 125  
 Val Ala Pro Thr Asp Ile Glu Glu Gly Met Arg Val Gly Val Asp Arg  
 130 135 140  
 Asn Lys Tyr Gln Ile His Ile Pro Leu Pro Pro Lys Ile Asp Pro Thr  
 145 150 155 160  
 Val Thr Met Met Gln Val Glu Glu Lys Pro Asp Val Thr Tyr Ser Asp  
 165 170 175  
 Val Gly Gly Cys Lys Glu Gln Ile Glu Lys Leu Arg Glu Val Val Glu  
 180 185 190  
 Thr Pro Leu Leu His Pro Glu Arg Phe Val Asn Leu Gly Ile Glu Pro  
 195 200 205  
 Pro Lys Gly Val Leu Leu Phe Gly Pro Pro Gly Thr Gly Lys Thr Leu  
 210 215 220  
 Cys Ala Arg Ala Val Ala Asn Arg Thr Asp Ala Cys Phe Ile Arg Val  
 225 230 235 240  
 Ile Gly Ser Glu Leu Val Gln Lys Tyr Val Gly Glu Gly Ala Arg Met  
 245 250 255  
 Val Arg Glu Leu Phe Glu Met Ala Arg Thr Lys Lys Ala Cys Leu Ile  
 260 265 270  
 Phe Phe Asp Glu Ile Asp Ala Ile Gly Gly Ala Arg Phe Asp Asp Gly  
 275 280 285  
 Ala Gly Gly Asp Asn Glu Val Gln Arg Thr Met Leu Glu Leu Ile Asn  
 290 295 300  
 Gln Leu Asp Gly Phe Asp Pro Arg Gly Asn Ile Lys Val Leu Met Ala  
 305 310 315 320  
 Thr Asn Arg Pro Asp Thr Leu Asp Pro Ala Leu Met Arg Pro Gly Arg  
 325 330 335  
 Leu Asp Arg Lys Ile Glu Phe Ser Leu Pro Asp Leu Glu Gly Arg Thr  
 340 345 350  
 His Ile Phe Lys Ile His Ala Arg Ser Met Ser Val Glu Arg Asp Ile  
 355 360 365  
 Arg Phe Glu Leu Leu Ala Arg Leu Cys Pro Asn Ser Thr Gly Ala Glu  
 370 375 380  
 Ile Arg Ser Val Cys Thr Glu Ala Gly Met Phe Ala Ile Arg Ala Arg  
 385 390 395 400  
 Arg Lys Ile Ala Thr Glu Lys Asp Phe Leu Glu Ala Val Asn Lys Val  
 405 410 415  
 Ile Lys Ser Tyr Ala Lys Phe Ser Ala Thr Pro Arg Tyr Met Thr Tyr  
 420 425 430  
 Asn

&lt;210&gt; 169

&lt;211&gt; 529

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens



<400> 169  
 Met Ser Thr Asn Glu Asn Ala Asn Thr Pro Ala Ala Arg Leu His Arg  
 1 5 10 15  
 Phe Lys Asn Lys Gly Lys Asp Ser Thr Glu Met Arg Arg Arg Ile  
 20 25 30  
 Glu Val Asn Val Glu Leu Arg Lys Ala Lys Lys Asp Asp Gln Met Leu  
 35 40 45  
 Lys Arg Arg Asn Val Ser Ser Phe Pro Asp Asp Ala Thr Ser Pro Leu  
 50 55 60  
 Gln Glu Asn Arg Asn Asn Gln Gly Thr Val Asn Trp Ser Val Asp Asp  
 65 70 75 80  
 Ile Val Lys Gly Ile Asn Ser Ser Asn Val Glu Asn Gln Leu Gln Ala  
 85 90 95  
 Thr Gln Ala Ala Arg Lys Leu Leu Ser Arg Glu Lys Gln Pro Pro Ile  
 100 105 110  
 Asp Asn Ile Ile Arg Ala Gly Leu Ile Pro Lys Phe Val Ser Phe Leu  
 115 120 125  
 Gly Arg Thr Asp Cys Ser Pro Ile Gln Phe Glu Ser Ala Trp Ala Leu  
 130 135 140  
 Thr Asn Ile Ala Ser Gly Thr Ser Glu Gln Thr Lys Ala Val Val Asp  
 145 150 155 160  
 Gly Gly Ala Ile Pro Ala Phe Ile Ser Leu Leu Ala Ser Pro His Ala  
 165 170 175  
 His Ile Ser Glu Gln Ala Val Trp Ala Leu Gly Asn Ile Ala Gly Asp  
 180 185 190  
 Gly Ser Val Phe Arg Asp Leu Val Ile Lys Tyr Gly Ala Val Asp Pro  
 195 200 205  
 Leu Leu Ala Leu Leu Ala Val Pro Asp Met Ser Ser Leu Ala Cys Gly  
 210 215 220  
 Tyr Leu Arg Asn Leu Thr Trp Thr Leu Ser Asn Leu Cys Arg Asn Lys  
 225 230 235 240  
 Asn Pro Ala Pro Pro Ile Asp Ala Val Glu Gln Ile Leu Pro Thr Leu  
 245 250 255  
 Val Arg Leu Leu His His Asp Asp Pro Glu Val Leu Ala Asp Thr Cys  
 260 265 270  
 Trp Ala Ile Ser Tyr Leu Thr Asp Gly Pro Asn Glu Arg Ile Gly Met  
 275 280 285  
 Val Val Lys Thr Gly Val Val Pro Gln Leu Val Lys Leu Leu Gly Ala  
 290 295 300  
 Ser Glu Leu Pro Ile Val Thr Pro Ala Leu Arg Ala Ile Gly Asn Ile  
 305 310 315 320  
 Val Thr Gly Thr Asp Glu Gln Thr Gln Val Val Ile Asp Ala Gly Ala  
 325 330 335  
 Leu Ala Val Phe Pro Ser Leu Leu Thr Asn Pro Lys Thr Asn Ile Gln  
 340 345 350  
 Lys Glu Ala Thr Trp Thr Met Ser Asn Ile Thr Ala Gly Arg Gln Asp  
 355 360 365  
 Gln Ile Gln Gln Val Val Asn His Gly Leu Val Pro Phe Leu Val Ser  
 370 375 380  
 Val Leu Ser Lys Ala Asp Phe Lys Thr Gln Lys Glu Ala Val Trp Ala  
 385 390 395 400  
 Val Thr Asn Tyr Thr Ser Gly Gly Thr Val Glu Gln Ile Val Tyr Leu  
 405 410 415  
 Val His Cys Gly Ile Ile Glu Pro Leu Met Asn Leu Leu Thr Ala Lys  
 420 425 430  
 Asp Thr Lys Ile Ile Leu Val Ile Leu Asp Ala Ile Ser Asn Ile Phe  
 435 440 445  
 Gln Ala Ala Glu Lys Leu Gly Glu Thr Glu Lys Leu Ser Ile Met Ile  
 450 455 460  
 Glu Glu Cys Gly Gly Leu Asp Lys Ile Glu Ala Leu Gln Asn His Glu  
 465 470 475 480

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Asn Glu Ser Val Tyr Lys Ala Ser Leu Ser Leu Ile Glu Lys Tyr Phe  
 485 490 495  
 Ser Val Glu Glu Glu Asp Gln Asn Val Val Pro Glu Thr Thr Ser  
 500 505 510  
 Glu Gly Tyr Thr Phe Gln Val Gln Asp Gly Ala Pro Gly Thr Phe Asn  
 515 520 525  
 Phe

&lt;210&gt; 170

&lt;211&gt; 971

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 170

Met Glu Leu Ser Asp Ala Asn Leu Gln Thr Leu Thr Glu Tyr Leu Lys  
 1 5 10 15  
 Lys Thr Leu Asp Pro Asp Pro Ala Ile Arg Arg Pro Ala Glu Lys Phe  
 20 25 30  
 Leu Glu Ser Val Glu Gly Asn Gln Asn Tyr Pro Leu Leu Leu Thr  
 35 40 45  
 Leu Leu Glu Lys Ser Gln Asp Asn Val Ile Lys Val Cys Ala Ser Val  
 50 55 60  
 Thr Phe Lys Asn Tyr Ile Lys Arg Asn Trp Arg Ile Val Glu Asp Glu  
 65 70 75 80  
 Pro Asn Lys Ile Cys Glu Ala Asp Arg Val Ala Ile Lys Ala Asn Ile  
 85 90 95  
 Val His Leu Met Leu Ser Ser Pro Glu Gln Ile Gln Lys Gln Leu Ser  
 100 105 110  
 Asp Ala Ile Ser Ile Ile Gly Arg Glu Asp Phe Pro Gln Lys Trp Pro  
 115 120 125  
 Asp Leu Leu Thr Glu Met Val Asn Arg Phe Gln Ser Gly Asp Phe His  
 130 135 140  
 Val Ile Asn Gly Val Leu Arg Thr Ala His Ser Leu Phe Lys Arg Tyr  
 145 150 155 160  
 Arg His Glu Phe Lys Ser Asn Glu Leu Trp Thr Glu Ile Lys Leu Val  
 165 170 175  
 Leu Asp Ala Phe Ala Leu Pro Leu Thr Asn Leu Phe Lys Ala Thr Ile  
 180 185 190  
 Glu Leu Cys Ser Thr His Ala Asn Asp Ala Ser Ala Leu Arg Ile Leu  
 195 200 205  
 Phe Ser Ser Leu Ile Leu Ile Ser Lys Leu Phe Tyr Ser Leu Asn Phe  
 210 215 220  
 Gln Asp Leu Pro Glu Phe Phe Glu Asp Asn Met Glu Thr Trp Met Asn  
 225 230 235 240  
 Asn Phe His Thr Leu Leu Thr Leu Asp Asn Lys Leu Leu Gln Thr Asp  
 245 250 255  
 Asp Glu Glu Glu Ala Gly Leu Leu Glu Leu Lys Ser Gln Ile Cys  
 260 265 270  
 Asp Asn Ala Ala Leu Tyr Ala Gln Lys Tyr Asp Glu Glu Phe Gln Arg  
 275 280 285  
 Tyr Leu Pro Arg Phe Val Thr Ala Ile Trp Asn Leu Leu Val Thr Thr  
 290 295 300  
 Gly Gln Glu Val Lys Tyr Asp Leu Leu Val Ser Asn Ala Ile Gln Phe  
 305 310 315 320  
 Leu Ala Ser Val Cys Glu Arg Pro His Tyr Lys Asn Leu Phe Glu Asp  
 325 330 335

Gln	Asn	Thr	Leu	Thr	Ser	Ile	Cys	Glu	Lys	Val	Ile	Val	Pro	Asn	Met
			340					345					350		
Glu	Phe	Arg	Ala	Ala	Asp	Glu	Glu	Ala	Phe	Glu	Asp	Asn	Ser	Glu	Glu
		355					360					365			
Tyr	Ile	Arg	Arg	Asp	Leu	Glu	Gly	Ser	Asp	Ile	Asp	Thr	Arg	Arg	Arg
	370					375					380				
Ala	Ala	Cys	Asp	Leu	Val	Arg	Gly	Leu	Cys	Lys	Phe	Phe	Glu	Gly	Pro
385					390					395					400
Val	Thr	Gly	Ile	Phe	Ser	Gly	Tyr	Val	Asn	Ser	Met	Leu	Gln	Glu	Tyr
				405					410					415	
Ala	Lys	Asn	Pro	Ser	Val	Asn	Trp	Lys	His	Lys	Asp	Ala	Ala	Ile	Tyr
			420					425					430		
Leu	Val	Thr	Ser	Leu	Ala	Ser	Lys	Ala	Gln	Thr	Gln	Lys	His	Gly	Ile
			435				440					445			
Thr	Gln	Ala	Asn	Glu	Leu	Val	Asn	Leu	Thr	Glu	Phe	Phe	Val	Asn	His
	450				455						460				
Ile	Leu	Pro	Asp	Leu	Lys	Ser	Ala	Asn	Val	Asn	Glu	Phe	Pro	Val	Leu
465					470					475					480
Lys	Ala	Asp	Gly	Ile	Lys	Tyr	Ile	Met	Ile	Phe	Arg	Asn	Gln	Val	Pro
				485					490					495	
Lys	Glu	His	Leu	Leu	Val	Ser	Ile	Pro	Leu	Leu	Ile	Asn	His	Leu	Gln
			500					505					510		
Ala	Glu	Ser	Ile	Val	Val	His	Thr	Tyr	Ala	Ala	His	Ala	Leu	Glu	Arg
		515					520					525			
Leu	Phe	Thr	Met	Arg	Gly	Pro	Asn	Asn	Ala	Thr	Leu	Phe	Thr	Ala	Ala
	530					535					540				
Glu	Ile	Ala	Pro	Phe	Val	Glu	Ile	Leu	Leu	Thr	Asn	Leu	Phe	Lys	Ala
545					550					555					560
Leu	Thr	Leu	Pro	Gly	Ser	Ser	Glu	Asn	Glu	Tyr	Ile	Met	Lys	Ala	Ile
				565					570					575	
Met	Arg	Ser	Phe	Ser	Leu	Leu	Gln	Glu	Ala	Ile	Ile	Pro	Tyr	Ile	Pro
			580					585					590		
Thr	Leu	Ile	Thr	Gln	Leu	Thr	Gln	Lys	Leu	Leu	Ala	Val	Ser	Lys	Asn
		595					600					605			
Pro	Ser	Lys	Pro	His	Phe	Asn	His	Tyr	Met	Phe	Glu	Ala	Ile	Cys	Leu
		610				615					620				
Ser	Ile	Arg	Ile	Thr	Cys	Lys	Ala	Asn	Pro	Ala	Ala	Val	Val	Asn	Phe
625					630					635					640
Glu	Glu	Ala	Leu	Phe	Leu	Val	Phe	Thr	Glu	Ile	Leu	Gln	Asn	Asp	Val
				645					650					655	
Gln	Glu	Phe	Ile	Pro	Tyr	Val	Phe	Gln	Val	Met	Ser	Leu	Leu	Leu	Glu
			660					665					670		
Thr	His	Lys	Asn	Asp	Ile	Pro	Ser	Ser	Tyr	Met	Ala	Leu	Phe	Pro	His
		675					680					685			
Leu	Leu	Gln	Pro	Val	Leu	Trp	Glu	Arg	Thr	Gly	Asn	Ile	Pro	Ala	Leu
		690				695					700				
Val	Arg	Leu	Leu	Gln	Ala	Phe	Leu	Glu	Arg	Gly	Ser	Asn	Thr	Ile	Ala
705					710					715					720
Ser	Ala	Ala	Ala	Asp	Lys	Ile	Pro	Gly	Leu	Gly	Val	Phe	Gln	Lys	
				725					730					735	
Leu	Ile	Ala	Ser	Lys	Ala	Asn	Asp	His	Gln	Gly	Phe	Tyr	Leu	Leu	Asn
			740					745					750		
Ser	Ile	Ile	Glu	His	Met	Pro	Pro	Glu	Ser	Val	Asp	Gln	Tyr	Arg	Lys
		755					760					765			
Gln	Ile	Phe	Ile	Leu	Leu	Phe	Gln	Arg	Leu	Gln	Asn	Ser	Lys	Thr	Thr
	770					775					780				
Lys	Phe	Ile	Lys	Ser	Phe	Leu	Val	Phe	Ile	Asn	Leu	Tyr	Cys	Ile	Lys
785					790					795					800
Tyr	Gly	Ala	Leu	Ala	Leu	Gln	Glu	Ile	Phe	Asp	Gly	Ile	Gln	Pro	Lys
				805					810					815	
Met	Phe	Gly	Met	Val	Leu	Glu	Lys	Ile	Ile	Ile	Pro	Glu	Ile	Gln	Lys
			820					825						830	

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Val Ser Gly Asn Val Glu Lys Lys Ile Cys Ala Val Gly Ile Thr Lys  
 835 840 845  
 Leu Leu Thr Glu Cys Pro Pro Met Met Asp Thr Glu Tyr Thr Lys Leu  
 850 855 860  
 Trp Thr Pro Leu Leu Gln Ser Leu Ile Gly Leu Phe Glu Leu Pro Glu  
 865 870 875 880  
 Asp Asp Thr Ile Pro Asp Glu Glu His Phe Ile Asp Ile Glu Asp Thr  
 885 890 895  
 Pro Gly Tyr Gln Thr Ala Phe Ser Gln Leu Ala Phe Ala Gly Lys Lys  
 900 905 910  
 Glu His Asp Pro Val Gly Gln Met Val Asn Asn Pro Lys Ile His Leu  
 915 920 925  
 Ala Gln Ser Leu His Lys Leu Ser Thr Ala Cys Pro Gly Arg Val Pro  
 930 935 940  
 Ser Met Val Ser Thr Ser Leu Asn Ala Glu Ala Leu Gln Tyr Leu Gln  
 945 950 955 960  
 Gly Tyr Leu Gln Ala Ala Ser Val Thr Leu Leu  
 965 970

&lt;210&gt; 171

&lt;211&gt; 184

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 171  
 Met Pro Gln Ser Lys Ser Arg Lys Ile Ala Ile Leu Gly Tyr Arg Ser  
 1 5 10 15  
 Val Gly Lys Ser Ser Leu Thr Ile Gln Phe Val Glu Gly Gln Phe Val  
 20 25 30  
 Asp Ser Tyr Asp Pro Thr Ile Glu Asn Thr Phe Thr Lys Leu Ile Thr  
 35 40 45  
 Val Asn Gly Gln Glu Tyr His Leu Gln Leu Val Asp Thr Ala Gly Gln  
 50 55 60  
 Asp Glu Tyr Ser Ile Phe Pro Gln Thr Tyr Ser Ile Asp Ile Asn Gly  
 65 70 75 80  
 Tyr Ile Leu Val Tyr Ser Val Thr Ser Ile Lys Ser Phe Glu Val Ile  
 85 90 95  
 Lys Val Ile His Gly Lys Leu Leu Asp Met Val Gly Lys Val Gln Ile  
 100 105 110  
 Pro Ile Met Leu Val Gly Asn Lys Lys Asp Leu His Met Glu Arg Val  
 115 120 125  
 Ile Ser Tyr Glu Glu Gly Lys Ala Leu Ala Glu Ser Trp Asn Ala Ala  
 130 135 140  
 Phe Leu Glu Ser Ser Ala Lys Glu Asn Gln Thr Ala Val Asp Val Phe  
 145 150 155 160  
 Arg Arg Ile Ile Leu Glu Ala Glu Lys Met Asp Gly Ala Ala Ser Gln  
 165 170 175  
 Gly Lys Ser Ser Cys Ser Val Met  
 180

&lt;210&gt; 172

&lt;211&gt; 514

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 172  
 Met Ala Asp Ala Glu Val Ile Ile Leu Pro Lys Lys His Lys Lys Lys  
 1 5 10 15  
 Lys Glu Arg Lys Ser Leu Pro Glu Glu Asp Val Ala Glu Ile Gln His  
 20 25 30  
 Ala Glu Glu Phe Leu Ile Lys Pro Glu Ser Lys Val Ala Lys Leu Asp  
 35 40 45  
 Thr Ser Gln Trp Pro Leu Leu Leu Lys Asn Phe Asp Lys Leu Asn Val  
 50 55 60  
 Arg Thr Thr His Tyr Thr Pro Leu Ala Cys Gly Ser Asn Pro Leu Lys  
 65 70 75 80  
 Arg Glu Ile Gly Asp Tyr Ile Arg Thr Gly Phe Ile Asn Leu Asp Lys  
 85 90 95  
 Pro Ser Asn Pro Ser Ser His Glu Val Val Ala Trp Ile Arg Arg Ile  
 100 105 110  
 Leu Arg Val Glu Lys Thr Gly His Ser Gly Thr Leu Asp Pro Lys Val  
 115 120 125  
 Thr Gly Cys Leu Ile Val Cys Ile Glu Arg Ala Thr Arg Leu Val Lys  
 130 135 140  
 Ser Gln Gln Ser Ala Gly Lys Glu Tyr Val Gly Ile Val Arg Leu His  
 145 150 155 160  
 Asn Ala Ile Glu Gly Gly Thr Gln Leu Ser Arg Ala Leu Glu Thr Leu  
 165 170 175  
 Thr Gly Ala Leu Phe Gln Arg Pro Pro Leu Ile Ala Ala Val Lys Arg  
 180 185 190  
 Gln Leu Arg Val Arg Thr Ile Tyr Glu Ser Lys Met Ile Glu Tyr Asp  
 195 200 205  
 Pro Glu Arg Arg Leu Gly Ile Phe Trp Val Ser Cys Glu Ala Gly Thr  
 210 215 220  
 Tyr Ile Arg Thr Leu Cys Val His Leu Gly Leu Leu Gly Val Gly  
 225 230 235 240  
 Gly Gln Met Gln Glu Leu Arg Arg Val Arg Ser Gly Val Met Ser Glu  
 245 250 255  
 Lys Asp His Met Val Thr Met His Asp Val Leu Asp Ala Gln Trp Leu  
 260 265 270  
 Tyr Asp Asn His Lys Asp Glu Ser Tyr Leu Arg Arg Val Val Tyr Pro  
 275 280 285  
 Leu Glu Lys Leu Leu Thr Ser His Lys Arg Leu Val Met Lys Asp Ser  
 290 295 300  
 Ala Val Asn Ala Ile Cys Tyr Gly Ala Lys Ile Met Leu Pro Gly Val  
 305 310 315 320  
 Leu Arg Tyr Glu Asp Gly Ile Glu Val Asn Gln Glu Ile Val Val Ile  
 325 330 335  
 Thr Thr Lys Gly Glu Ala Ile Cys Met Ala Ile Ala Leu Met Thr Thr  
 340 345 350  
 Ala Val Ile Ser Thr Cys Asp His Gly Ile Val Ala Lys Ile Lys Arg  
 355 360 365  
 Val Ile Met Glu Arg Asp Thr Tyr Pro Arg Lys Trp Gly Leu Gly Pro  
 370 375 380  
 Lys Ala Ser Gln Lys Lys Leu Met Ile Lys Gln Gly Leu Leu Asp Lys  
 385 390 395 400  
 His Gly Lys Pro Thr Asp Ser Thr Pro Ala Thr Trp Lys Gln Glu Tyr  
 405 410 415  
 Val Asp Tyr Ser Glu Ser Ala Lys Lys Glu Val Val Ala Glu Val Val  
 420 425 430  
 Lys Ala Pro Gln Val Val Ala Glu Ala Ala Lys Thr Ala Lys Arg Lys  
 435 440 445  
 Arg Glu Ser Glu Ser Glu Ser Asp Glu Thr Pro Pro Ala Ala Pro Gln  
 450 455 460

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Leu Ile Lys Lys Glu Lys Lys Lys Ser Lys Lys Asp Lys Lys Ala Lys  
 465 470 475 480  
 Ala Gly Leu Glu Ser Gly Ala Glu Pro Gly Asp Gly Asp Ser Asp Thr  
 485 490 495  
 Thr Lys Lys Lys Lys Lys Lys Lys Lys Ala Lys Glu Val Glu Leu Val  
 500 505 510  
 Ser Glu

&lt;210&gt; 173

&lt;211&gt; 258

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 173

Met Leu Pro Leu Cys Leu Val Ala Ala Leu Leu Leu Ala Ala Gly Pro  
 1 5 10 15  
 Gly Pro Ser Leu Gly Asp Glu Ala Ile His Cys Pro Pro Cys Ser Glu  
 20 25 30  
 Glu Lys Leu Ala Arg Cys Arg Pro Pro Val Gly Cys Glu Glu Leu Val  
 35 40 45  
 Arg Glu Ala Gly Cys Gly Cys Cys Ala Thr Cys Ala Leu Gly Leu Gly  
 50 55 60  
 Met Pro Cys Gly Val Tyr Thr Pro Arg Cys Gly Ser Gly Leu Arg Cys  
 65 70 75 80  
 Tyr Pro Pro Arg Gly Val Glu Lys Pro Leu His Thr Leu Met His Gly  
 85 90 95  
 Gln Gly Val Cys Met Glu Leu Ala Glu Ile Glu Ala Ile Gln Glu Ser  
 100 105 110  
 Leu Gln Pro Ser Asp Lys Asp Glu Gly Asp His Pro Asn Asn Ser Phe  
 115 120 125  
 Ser Pro Cys Ser Ala His Asp Arg Arg Cys Leu Gln Lys His Phe Ala  
 130 135 140  
 Lys Ile Arg Asp Arg Ser Thr Ser Gly Gly Lys Met Lys Val Asn Gly  
 145 150 155 160  
 Ala Pro Arg Glu Asp Ala Arg Pro Val Pro Gln Gly Ser Cys Gln Ser  
 165 170 175  
 Glu Leu His Arg Ala Leu Glu Arg Leu Ala Ala Ser Gln Ser Arg Thr  
 180 185 190  
 His Glu Asp Leu Tyr Phe Ile Pro Ile Pro Asn Cys Asp Arg Asn Gly  
 195 200 205  
 Asn Phe His Pro Lys Gln Cys His Pro Ala Leu Asp Gly Gln Arg Gly  
 210 215 220  
 Lys Cys Trp Cys Val Asp Arg Lys Thr Gly Val Lys Leu Pro Gly Gly  
 225 230 235 240  
 Leu Glu Pro Lys Gly Glu Leu Asp Cys His Gln Leu Ala Asp Ser Phe  
 245 250 255  
 Arg Glu

&lt;210&gt; 174

&lt;211&gt; 1233

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 174  
 Met Gly Phe Leu Lys Leu Ile Glu Ile Glu Asn Phe Lys Ser Tyr Lys  
 1 5 10 15  
 Gly Arg Gln Ile Ile Gly Pro Phe Gln Arg Phe Thr Ala Ile Ile Gly  
 20 25 30  
 Pro Asn Gly Ser Gly Lys Ser Asn Leu Met Asp Ala Ile Ser Phe Val  
 35 40 45  
 Leu Gly Glu Lys Thr Ser Asn Leu Arg Val Lys Thr Leu Arg Asp Leu  
 50 55 60  
 Ile His Gly Ala Pro Val Gly Lys Pro Ala Ala Asn Arg Ala Phe Val  
 65 70 75 80  
 Ser Met Val Tyr Ser Glu Glu Gly Ala Glu Asp Arg Thr Phe Ala Arg  
 85 90 95  
 Val Ile Val Gly Gly Ser Ser Glu Tyr Lys Ile Asn Asn Lys Val Val  
 100 105 110  
 Gln Leu His Glu Tyr Ser Glu Glu Leu Glu Lys Leu Gly Ile Leu Ile  
 115 120 125  
 Lys Ala Arg Asn Phe Leu Val Phe Gln Gly Ala Val Glu Ser Ile Ala  
 130 135 140  
 Met Lys Asn Pro Lys Glu Arg Thr Ala Leu Phe Glu Glu Ile Ser Arg  
 145 150 155 160  
 Ser Gly Glu Leu Ala Gln Glu Tyr Asp Lys Arg Lys Lys Glu Met Val  
 165 170 175  
 Lys Ala Glu Glu Asp Thr Gln Phe Asn Tyr His Arg Lys Lys Asn Ile  
 180 185 190  
 Ala Ala Glu Arg Lys Glu Ala Lys Gln Glu Lys Glu Glu Ala Asp Arg  
 195 200 205  
 Tyr Gln Arg Leu Lys Asp Glu Val Val Arg Ala Gln Val Gln Leu Gln  
 210 215 220  
 Leu Phe Lys Leu Tyr His Asn Glu Val Glu Ile Glu Lys Leu Asn Lys  
 225 230 235 240  
 Glu Leu Ala Ser Lys Asn Lys Glu Ile Glu Lys Asp Lys Lys Arg Met  
 245 250 255  
 Asp Lys Val Glu Asp Glu Leu Lys Glu Lys Lys Lys Glu Leu Gly Lys  
 260 265 270  
 Met Met Arg Glu Gln Gln Gln Ile Glu Lys Glu Ile Lys Glu Lys Asp  
 275 280 285  
 Ser Glu Leu Asn Gln Lys Arg Pro Gln Tyr Ile Lys Ala Lys Glu Asn  
 290 295 300  
 Thr Ser His Lys Ile Lys Lys Leu Glu Ala Ala Lys Lys Ser Leu Gln  
 305 310 315 320  
 Asn Ala Gln Lys His Tyr Lys Lys Arg Lys Gly Asp Met Asp Glu Leu  
 325 330 335  
 Glu Lys Glu Met Leu Ser Val Glu Lys Ala Arg Gln Glu Phe Glu Glu  
 340 345 350  
 Arg Met Glu Glu Glu Ser Gln Ser Gln Gly Arg Asp Leu Thr Leu Glu  
 355 360 365  
 Glu Asn Gln Val Lys Lys Tyr His Arg Leu Lys Glu Glu Ala Ser Lys  
 370 375 380  
 Arg Ala Ala Thr Leu Ala Gln Glu Leu Glu Lys Phe Asn Arg Asp Gln  
 385 390 395 400  
 Lys Ala Asp Gln Asp Arg Leu Asp Leu Glu Glu Arg Lys Lys Val Glu  
 405 410 415  
 Thr Glu Ala Lys Ile Lys Gln Lys Leu Arg Glu Ile Glu Glu Asn Gln  
 420 425 430  
 Lys Arg Ile Glu Lys Leu Glu Glu Tyr Ile Thr Thr Ser Lys Gln Ser  
 435 440 445  
 Leu Glu Glu Gln Lys Lys Leu Glu Gly Glu Leu Thr Glu Glu Val Glu  
 450 455 460

Met Ala Lys Arg Arg Ile Asp Glu Ile Asn Lys Glu Leu Asn Gln Val  
 465 470 475 480  
 Met Glu Gln Leu Gly Asp Ala Arg Ile Asp Arg Gln Glu Ser Ser Arg  
 485 490 495  
 Gln Gln Arg Lys Ala Glu Ile Met Glu Ser Ile Lys Arg Leu Tyr Pro  
 500 505 510  
 Gly Ser Val Tyr Gly Arg Leu Ile Asp Leu Cys Gln Pro Thr Gln Lys  
 515 520 525  
 Lys Tyr Gln Ile Ala Val Thr Lys Val Leu Gly Lys Asn Met Asp Ala  
 530 535 540  
 Ile Ile Val Asp Ser Glu Lys Thr Gly Arg Asp Cys Ile Gln Tyr Ile  
 545 550 555 560  
 Lys Glu Gln Arg Gly Glu Pro Glu Thr Phe Leu Pro Leu Asp Tyr Leu  
 565 570 575  
 Glu Val Lys Pro Thr Asp Glu Lys Leu Arg Glu Leu Lys Gly Ala Lys  
 580 585 590  
 Leu Val Ile Asp Val Ile Arg Tyr Glu Pro Pro His Ile Lys Lys Ala  
 595 600 605  
 Leu Gln Tyr Ala Cys Gly Asn Ala Leu Val Cys Asp Asn Val Glu Asp  
 610 615 620  
 Ala Arg Arg Ile Ala Phe Gly Gly His Gln Arg His Lys Thr Val Ala  
 625 630 635 640  
 Leu Asp Gly Thr Leu Phe Gln Lys Ser Gly Val Ile Ser Gly Gly Ala  
 645 650 655  
 Ser Asp Leu Lys Ala Lys Ala Arg Arg Trp Asp Glu Lys Ala Val Asp  
 660 665 670  
 Lys Leu Lys Glu Lys Lys Glu Arg Leu Thr Glu Glu Leu Lys Glu Gln  
 675 680 685  
 Met Lys Ala Lys Arg Lys Glu Ala Glu Leu Arg Gln Val Gln Ser Gln  
 690 695 700  
 Ala His Gly Leu Gln Met Arg Leu Lys Tyr Ser Gln Ser Asp Leu Glu  
 705 710 715 720  
 Gln Thr Lys Thr Arg His Leu Ala Leu Asn Leu Gln Glu Lys Ser Lys  
 725 730 735  
 Leu Glu Ser Glu Leu Ala Asn Phe Gly Pro Arg Ile Asn Asp Ile Lys  
 740 745 750  
 Arg Ile Ile Gln Ser Arg Glu Arg Glu Met Lys Asp Leu Lys Glu Lys  
 755 760 765  
 Met Asn Gln Val Glu Asp Glu Val Phe Glu Glu Phe Cys Arg Glu Ile  
 770 775 780  
 Gly Val Arg Asn Ile Arg Glu Phe Glu Glu Glu Lys Val Lys Arg Gln  
 785 790 795 800  
 Asn Glu Ile Ala Lys Lys Arg Leu Glu Phe Glu Asn Gln Lys Thr Arg  
 805 810 815  
 Leu Gly Ile Gln Leu Asp Phe Glu Lys Asn Gln Leu Lys Glu Asp Gln  
 820 825 830  
 Asp Lys Val His Met Trp Glu Gln Thr Val Lys Lys Asp Glu Asn Glu  
 835 840 845  
 Ile Glu Lys Leu Lys Lys Glu Glu Gln Arg His Met Lys Ile Ile Asp  
 850 855 860  
 Glu Thr Met Ala Gln Leu Glu Asp Leu Lys Asn Gln His Leu Ala Lys  
 865 870 875 880  
 Lys Ser Glu Val Asn Asp Lys Asn His Glu Met Glu Glu Ile Arg Lys  
 885 890 895  
 Lys Leu Gly Gly Ala Asn Lys Glu Met Thr His Leu Gln Lys Glu Val  
 900 905 910  
 Thr Ala Ile Glu Thr Lys Leu Glu Gln Lys Arg Ser Asp Arg His Asn  
 915 920 925  
 Leu Leu Gln Ala Cys Lys Met Gln Asp Ile Lys Leu Pro Leu Ser Lys  
 930 935 940  
 Gly Thr Met Asp Asp Ile Ser Gln Glu Glu Gly Ser Ser Gln Gly Glu  
 945 950 955 960



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[illegible]

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Glu Ser Leu Leu Gly Leu Thr Val Tyr Gly Ser Asn Asp Gln Asp Pro  
 115 120 125  
 Tyr Val Thr Leu Lys Asp Thr Glu Gln Tyr Glu Arg Glu Asp Phe Leu  
 130 135 140  
 Ile Lys Pro Ser Asp Asn Leu Ile Val Cys Gly Arg Ala Glu Gln Asp  
 145 150 155 160  
 Gln Cys Asn Leu Glu Val His Val Tyr Asn Gln Glu Glu Asp Ser Phe  
 165 170 175  
 Tyr Val His His Asp Ile Leu Leu Ser Ala Tyr Pro Leu Ser Val Glu  
 180 185 190  
 Trp Leu Asn Phe Asp Pro Ser Pro Asp Asp Ser Thr Gly Asn Tyr Ile  
 195 200 205  
 Ala Val Gly Asn Met Thr Pro Val Ile Glu Val Trp Asp Leu Asp Ile  
 210 215 220  
 Val Asp Ser Leu Glu Pro Val Phe Thr Leu Gly Ser Lys Leu Ser Lys  
 225 230 235 240  
 Lys Lys Lys Lys Lys Gly Lys Lys Ser Ser Ser Ala Glu Gly His Thr  
 245 250 255  
 Asp Ala Val Leu Asp Leu Ser Trp Asn Lys Leu Ile Arg Asn Val Leu  
 260 265 270  
 Ala Ser Ala Ser Ala Asp Asn Thr Val Ile Leu Trp Asp Met Ser Leu  
 275 280 285  
 Gly Lys Pro Ala Ala Ser Leu Ala Val His Thr Asp Lys Val Gln Thr  
 290 295 300  
 Leu Gln Phe His Pro Phe Glu Ala Gln Thr Leu Ile Ser Gly Ser Tyr  
 305 310 315 320  
 Asp Lys Ser Val Ala Leu Tyr Asp Cys Arg Ser Pro Asp Glu Ser His  
 325 330 335  
 Arg Met Trp Arg Phe Ser Gly Gln Ile Glu Arg Val Thr Trp Asn His  
 340 345 350  
 Phe Ser Pro Cys His Phe Leu Ala Ser Thr Asp Asp Gly Phe Val Tyr  
 355 360 365  
 Asn Leu Asp Ala Arg Ser Asp Lys Pro Ile Phe Thr Leu Asn Ala His  
 370 375 380  
 Asn Asp Glu Ile Ser Gly Leu Asp Leu Ser Ser Gln Ile Lys Gly Cys  
 385 390 395 400  
 Leu Val Thr Ala Ser Ala Asp Lys Tyr Val Lys Ile Trp Asp Ile Leu  
 405 410 415  
 Gly Asp Arg Pro Ser Leu Val His Ser Arg Asp Met Lys Met Gly Val  
 420 425 430  
 Leu Phe Cys Ser Ser Cys Cys Pro Asp Leu Pro Phe Ile Tyr Ala Phe  
 435 440 445  
 Gly Gly Gln Lys Glu Gly Leu Arg Val Trp Asp Ile Ser Thr Val Ser  
 450 455 460  
 Ser Val Asn Glu Ala Phe Gly Arg Arg Glu Arg Leu Val Leu Gly Ser  
 465 470 475 480  
 Ala Arg Asn Ser Ser Ile Ser Gly Pro Phe Gly Ser Arg Ser Ser Asp  
 485 490 495  
 Thr Pro Met Glu Ser  
 500

&lt;210&gt; 176

&lt;211&gt; 488

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 176  
 Met Ala Tyr Ser Gln Gly Gly Gly Lys Lys Lys Val Cys Tyr Tyr Tyr  
 1 5 10 15  
 Asp Gly Asp Ile Gly Asn Tyr Tyr Tyr Gly Gln Gly His Pro Met Lys  
 20 25 30  
 Pro His Arg Ile Arg Met Thr His Asn Leu Leu Leu Asn Tyr Gly Leu  
 35 40 45  
 Tyr Arg Lys Met Glu Ile Tyr Arg Pro His Lys Ala Thr Ala Glu Glu  
 50 55 60  
 Met Thr Lys Tyr His Ser Asp Glu Tyr Ile Lys Phe Leu Arg Ser Ile  
 65 70 75 80  
 Arg Pro Asp Asn Met Ser Glu Tyr Ser Lys Gln Met His Ile Phe Asn  
 85 90 95  
 Val Gly Glu Asp Cys Pro Ala Phe Asp Gly Leu Phe Glu Phe Cys Gln  
 100 105 110  
 Leu Ser Thr Gly Gly Ser Val Ala Gly Ala Val Lys Leu Asn Arg Gln  
 115 120 125  
 Gln Thr Asp Met Ala Val Asn Trp Ala Gly Gly Leu His His Ala Lys  
 130 135 140  
 Lys Tyr Glu Ala Ser Gly Phe Cys Tyr Val Asn Asp Ile Val Leu Ala  
 145 150 155 160  
 Ile Leu Glu Leu Leu Lys Tyr His Gln Arg Val Leu Tyr Ile Asp Ile  
 165 170 175  
 Asp Ile His His Gly Asp Gly Val Glu Glu Ala Phe Tyr Thr Asp  
 180 185 190  
 Arg Val Met Thr Val Ser Phe His Lys Tyr Gly Glu Tyr Phe Pro Gly  
 195 200 205  
 Thr Gly Asp Leu Arg Asp Ile Gly Ala Gly Lys Gly Lys Tyr Tyr Ala  
 210 215 220  
 Val Asn Phe Pro Met Cys Asp Gly Ile Asp Asp Glu Ser Tyr Gly Gln  
 225 230 235 240  
 Ile Phe Lys Pro Ile Ser Lys Val Met Glu Met Tyr Gln Pro Ser  
 245 250 255  
 Ala Val Val Leu Gln Cys Gly Ala Asp Ser Leu Ser Gly Asp Arg Leu  
 260 265 270  
 Gly Cys Phe Asn Leu Thr Val Lys Gly His Ala Lys Cys Val Glu Val  
 275 280 285  
 Val Lys Thr Phe Asn Leu Pro Leu Leu Met Leu Gly Gly Gly Tyr  
 290 295 300  
 Thr Ile Arg Asn Val Ala Arg Cys Trp Thr Tyr Glu Thr Ala Val Ala  
 305 310 315 320  
 Leu Asp Cys Glu Ile Pro Asn Glu Leu Pro Tyr Asn Asp Tyr Phe Glu  
 325 330 335  
 Tyr Phe Gly Pro Asp Phe Lys Leu His Ile Ser Pro Ser Asn Met Thr  
 340 345 350  
 Asn Gln Asn Thr Pro Glu Tyr Met Glu Lys Ile Lys Gln Arg Leu Phe  
 355 360 365  
 Glu Asn Leu Arg Met Leu Pro His Ala Pro Gly Val Gln Met Gln Ala  
 370 375 380  
 Ile Pro Glu Asp Ala Val His Glu Asp Ser Gly Asp Glu Asp Gly Glu  
 385 390 395 400  
 Asp Pro Asp Lys Arg Ile Ser Ile Arg Ala Ser Asp Lys Arg Ile Ala  
 405 410 415  
 Cys Asp Glu Glu Phe Ser Asp Ser Glu Asp Glu Gly Glu Gly Arg  
 420 425 430  
 Arg Asn Val Ala Asp His Lys Lys Gly Ala Lys Lys Ala Arg Ile Glu  
 435 440 445  
 Glu Asp Lys Lys Glu Thr Glu Asp Lys Lys Thr Asp Val Lys Glu Glu  
 450 455 460

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Asp Lys Ser Lys Asp Asn Ser Gly Glu Lys Thr Asp Thr Lys Gly Thr  
 465 470 475 480  
 Lys Ser Glu Gln Leu Ser Asn Pro

&lt;210&gt; 177

&lt;211&gt; 270

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 177

Met Gly Asn Thr Ser Ser Glu Arg Ala Ala Leu Glu Arg His Gly Gly  
 1 5 10 15  
 His Lys Thr Pro Arg Arg Asp Ser Ser Gly Gly Thr Lys Asp Gly Asp  
 20 25 30  
 Arg Pro Lys Ile Leu Met Asp Ser Pro Glu Asp Ala Asp Leu Phe His  
 35 40 45  
 Ser Glu Glu Ile Lys Ala Pro Glu Lys Glu Glu Phe Leu Ala Trp Gln  
 50 55 60  
 His Asp Leu Glu Val Asn Asp Lys Ala Pro Ala Gln Ala Arg Pro Thr  
 65 70 75 80  
 Val Phe Arg Trp Thr Gly Gly Gly Lys Glu Val Tyr Leu Ser Gly Ser  
 85 90 95  
 Phe Asn Asn Trp Ser Lys Leu Pro Leu Thr Arg Ser His Asn Asn Phe  
 100 105 110  
 Val Ala Ile Leu Asp Leu Pro Glu Gly Glu His Gln Tyr Lys Phe Phe  
 115 120 125  
 Val Asp Gly Gln Trp Thr His Asp Pro Ser Glu Pro Ile Val Thr Ser  
 130 135 140  
 Gln Leu Gly Thr Val Asn Asn Ile Ile Gln Val Lys Lys Thr Asp Phe  
 145 150 155 160  
 Glu Val Phe Asp Ala Leu Met Val Asp Ser Gln Lys Cys Ser Asp Val  
 165 170 175  
 Ser Glu Leu Ser Ser Ser Pro Pro Gly Pro Tyr His Gln Glu Pro Tyr  
 180 185 190  
 Val Cys Lys Pro Glu Glu Arg Phe Arg Ala Pro Pro Ile Leu Pro Pro  
 195 200 205  
 His Leu Leu Gln Val Ile Leu Asn Lys Asp Thr Gly Ile Ser Cys Asp  
 210 215 220  
 Pro Ala Leu Leu Pro Glu Pro Asn His Val Met Leu Asn His Leu Tyr  
 225 230 235 240  
 Ala Leu Ser Ile Lys Asp Gly Val Met Val Leu Ser Ala Thr His Arg  
 245 250 255  
 Tyr Lys Lys Lys Tyr Val Thr Thr Leu Leu Tyr Lys Pro Ile  
 260 265 270

&lt;210&gt; 178

&lt;211&gt; 514

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 178

Met Ala Asp Tyr Leu Ile Ser Gly Gly Thr Ser Tyr Val Pro Asp Asp  
 1 5 10 15

Gly	Leu	Thr	Ala	Gln	Gln	Leu	Phe	Asn	Cys	Gly	Asp	Gly	Leu	Thr	Tyr
			20					25					30		
Asn	Asp	Phe	Leu	Ile	Leu	Pro	Gly	Tyr	Ile	Asp	Phe	Thr	Ala	Asp	Gln
		35					40					45			
Val	Asp	Leu	Thr	Ser	Ala	Leu	Thr	Lys	Lys	Ile	Thr	Leu	Lys	Thr	Pro
	50					55					60				
Leu	Val	Ser	Ser	Pro	Met	Asp	Thr	Val	Thr	Glu	Ala	Gly	Met	Ala	Ile
	65				70					75					80
Ala	Met	Ala	Leu	Thr	Gly	Gly	Ile	Gly	Phe	Ile	His	His	Asn	Cys	Thr
				85					90				95		
Pro	Glu	Phe	Gln	Ala	Asn	Glu	Val	Arg	Lys	Val	Lys	Lys	Tyr	Glu	Gln
			100					105					110		
Gly	Phe	Ile	Thr	Asp	Pro	Val	Val	Leu	Ser	Pro	Lys	Asp	Arg	Val	Arg
		115					120					125			
Asp	Val	Phe	Glu	Ala	Lys	Ala	Arg	His	Gly	Phe	Cys	Gly	Ile	Pro	Ile
	130					135					140				
Thr	Asp	Thr	Gly	Arg	Met	Gly	Ser	Arg	Leu	Val	Gly	Ile	Ile	Ser	Ser
	145				150					155					160
Arg	Asp	Ile	Asp	Phe	Leu	Lys	Glu	Glu	Glu	His	Asp	Cys	Phe	Leu	Glu
				165					170					175	
Glu	Ile	Met	Thr	Lys	Arg	Glu	Asp	Leu	Val	Val	Ala	Pro	Arg	Ser	Ile
			180					185					190		
Thr	Leu	Lys	Glu	Ala	Asn	Glu	Ile	Leu	Gln	Arg	Ser	Lys	Lys	Gly	Lys
		195					200					205			
Leu	Pro	Ile	Val	Asn	Glu	Asp	Glu	Leu	Val	Ala	Ile	Ile	Ala	Arg	
	210					215					220				
Thr	Asp	Leu	Lys	Lys	Asn	Arg	Asp	Tyr	Pro	Leu	Ala	Ser	Lys	Asp	Ala
	225				230					235					240
Lys	Lys	Gln	Leu	Leu	Cys	Gly	Ala	Ala	Ile	Gly	Thr	His	Glu	Asp	Asp
				245					250				255		
Lys	Tyr	Arg	Leu	Asp	Leu	Leu	Ala	Gln	Ala	Gly	Val	Asp	Val	Val	Val
			260						265				270		
Leu	Asp	Ser	Ser	Gln	Gly	Asn	Ser	Ile	Phe	Gln	Ile	Asn	Met	Ile	Lys
		275				280						285			
Tyr	Ile	Lys	Asp	Lys	Tyr	Pro	Asn	Leu	Gln	Val	Ile	Gly	Gly	Asn	Val
	290					295					300				
Val	Thr	Ala	Ala	Gln	Ala	Lys	Asn	Leu	Ile	Asp	Ala	Gly	Val	Asp	Ala
	305				310					315					320
Leu	Arg	Val	Gly	Met	Gly	Ser	Gly	Ser	Ile	Cys	Ile	Thr	Gln	Glu	Val
				325					330				335		
Leu	Ala	Cys	Gly	Arg	Pro	Gln	Ala	Thr	Ala	Val	Tyr	Lys	Val	Ser	Glu
			340					345					350		
Tyr	Ala	Arg	Arg	Phe	Gly	Val	Pro	Val	Ile	Ala	Asp	Gly	Gly	Ile	Gln
		355					360					365			
Asn	Val	Gly	His	Ile	Ala	Lys	Ala	Leu	Ala	Leu	Gly	Ala	Ser	Thr	Val
	370					375					380				
Met	Met	Gly	Ser	Leu	Leu	Ala	Ala	Thr	Thr	Glu	Ala	Pro	Gly	Glu	Tyr
	385				390					395					400
Phe	Phe	Ser	Asp	Gly	Ile	Arg	Leu	Lys	Lys	Tyr	Arg	Gly	Met	Gly	Ser
				405					410					415	
Leu	Asp	Ala	Met	Asp	Lys	His	Leu	Ser	Ser	Gln	Asn	Arg	Tyr	Phe	Ser
			420					425					430		
Glu	Ala	Asp	Lys	Ile	Lys	Val	Ala	Gln	Gly	Val	Ser	Gly	Ala	Val	Gln
		435					440					445			
Asp	Lys	Gly	Ser	Ile	His	Lys	Phe	Val	Pro	Tyr	Leu	Ile	Ala	Gly	Ile
	450					455					460				
Gln	His	Ser	Cys	Gln	Asp	Ile	Gly	Ala	Lys	Ser	Leu	Thr	Gln	Val	Arg
	465				470					475					480
Ala	Met	Met	Tyr	Ser	Gly	Glu	Leu	Lys	Phe	Glu	Lys	Arg	Thr	Ser	Ser
				485					490					495	
Ala	Gln	Val	Glu	Gly	Gly	Val	His	Ser	Leu	His	Ser	Tyr	Glu	Lys	Arg
			500					505					510		

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Leu Phe

&lt;210&gt; 179

&lt;211&gt; 152

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 179

Met	Ser	Thr	Pro	Ala	Arg	Arg	Arg	Leu	Met	Arg	Asp	Phe	Lys	Arg	Leu
1				5					10					15	
Gln	Glu	Asp	Pro	Pro	Ala	Gly	Val	Ser	Gly	Ala	Pro	Ser	Glu	Asn	Asn
			20					25					30		
Ile	Met	Val	Trp	Asn	Ala	Val	Ile	Phe	Gly	Pro	Glu	Gly	Thr	Pro	Phe
		35					40					45			
Glu	Asp	Gly	Thr	Phe	Lys	Leu	Thr	Ile	Glu	Phe	Thr	Glu	Glu	Tyr	Pro
	50					55					60				
Asn	Lys	Pro	Pro	Thr	Val	Arg	Phe	Val	Ser	Lys	Met	Phe	His	Pro	Asn
65					70					75					80
Val	Tyr	Ala	Asp	Gly	Ser	Ile	Cys	Leu	Asp	Ile	Leu	Gln	Asn	Arg	Trp
				85					90				95		
Ser	Pro	Thr	Tyr	Asp	Val	Ser	Ser	Ile	Leu	Thr	Ser	Ile	Gln	Ser	Leu
			100					105					110		
Leu	Asp	Glu	Pro	Asn	Pro	Asn	Ser	Pro	Ala	Asn	Ser	Gln	Ala	Ala	Gln
		115					120					125			
Leu	Tyr	Gln	Glu	Asn	Lys	Arg	Glu	Tyr	Glu	Lys	Arg	Val	Ser	Ala	Ile
	130					135					140				
Val	Glu	Gln	Ser	Trp	Arg	Asp	Cys								
145					150										

&lt;210&gt; 180

&lt;211&gt; 260

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 180

Met	Pro	Gln	Asn	Glu	Tyr	Ile	Glu	Leu	His	Arg	Lys	Arg	Tyr	Gly	Tyr
1				5					10					15	
Arg	Leu	Asp	Tyr	His	Glu	Lys	Lys	Arg	Lys	Lys	Glu	Ser	Arg	Glu	Ala
			20					25					30		
His	Glu	Arg	Ser	Lys	Lys	Ala	Lys	Lys	Met	Ile	Gly	Leu	Lys	Ala	Lys
		35					40					45			
Leu	Tyr	His	Lys	Gln	Arg	His	Ala	Glu	Lys	Ile	Gln	Met	Lys	Lys	Thr
	50					55					60				
Ile	Lys	Met	His	Glu	Lys	Arg	Asn	Thr	Lys	Gln	Lys	Asn	Asp	Glu	Lys
65					70					75				80	
Thr	Pro	Gln	Gly	Ala	Val	Pro	Ala	Tyr	Leu	Leu	Asp	Arg	Glu	Gly	Gln
			85					90					95		
Ser	Arg	Ala	Lys	Val	Leu	Ser	Asn	Met	Ile	Lys	Gln	Lys	Arg	Lys	Glu
			100					105					110		
Lys	Ala	Gly	Lys	Trp	Glu	Val	Pro	Leu	Pro	Lys	Val	Arg	Ala	Gln	Gly
		115					120					125			
Glu	Thr	Glu	Val	Leu	Lys	Val	Ile	Arg	Thr	Gly	Lys	Arg	Lys	Lys	Lys
	130					135					140				

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Ala Trp Lys Arg Met Val Thr Lys Val Cys Phe Val Gly Asp Gly Phe  
 145 150 155 160  
 Thr Arg Lys Pro Pro Lys Tyr Glu Arg Phe Ile Arg Pro Met Gly Leu  
 165 170 175  
 Arg Phe Lys Lys Ala His Val Thr His Pro Glu Leu Lys Ala Thr Phe  
 180 185 190  
 Cys Leu Pro Ile Leu Gly Val Lys Lys Asn Pro Ser Ser Pro Leu Tyr  
 195 200 205  
 Thr Thr Leu Gly Val Ile Thr Lys Gly Thr Val Ile Glu Val Asn Val  
 210 215 220  
 Ser Glu Leu Gly Leu Val Thr Gln Gly Gly Lys Val Ile Trp Gly Lys  
 225 230 235 240  
 Tyr Ala Gln Val Thr Asn Asn Pro Glu Asn Asp Gly Cys Ile Asn Ala  
 245 250 255  
 Val Leu Leu Val  
 260

&lt;210&gt; 181

&lt;211&gt; 790

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 181

Met Glu Ala Thr Ser Arg Glu Ala Ala Pro Ala Lys Ser Ser Ala Ser  
 1 5 10 15  
 Gly Pro Asn Ala Pro Pro Ala Leu Phe Glu Leu Cys Gly Arg Ala Val  
 20 25 30  
 Ser Ala His Met Gly Val Leu Glu Ser Gly Val Trp Ala Leu Pro Gly  
 35 40 45  
 Pro Ile Leu Gln Ser Ile Leu Pro Leu Leu Asn Ile Tyr Tyr Leu Glu  
 50 55 60  
 Arg Ile Glu Glu Thr Ala Leu Lys Lys Gly Leu Ser Thr Gln Ala Ile  
 65 70 75 80  
 Trp Arg Arg Leu Trp Asp Glu Leu Met Lys Thr Arg Pro Ser Ser Leu  
 85 90 95  
 Glu Ser Val Thr Cys Trp Arg Ala Lys Phe Met Glu Ala Phe Phe Ser  
 100 105 110  
 His Val Leu Arg Gly Thr Ile Asp Val Ser Ser Asp Arg Arg Leu Cys  
 115 120 125  
 Asp Gln Arg Phe Ser Pro Leu Leu His Ser Ser Arg His Val Arg Gln  
 130 135 140  
 Leu Thr Ile Cys Asn Met Leu Gln Gly Ala Thr Glu Leu Val Ala Glu  
 145 150 155 160  
 Pro Asn Arg Arg Val Leu Glu Thr Leu Ala Ser Ser Leu His Thr Leu  
 165 170 175  
 Lys Phe Arg His Leu Leu Phe Ser Asp Val Ala Ala Gln Gln Ser Leu  
 180 185 190  
 Arg Gln Leu Leu His Gln Leu Ile His His Gly Ala Val Ser Gln Val  
 195 200 205  
 Ser Leu Tyr Ser Trp Pro Val Pro Glu Ser Ala Leu Phe Ile Leu Ile  
 210 215 220  
 Leu Thr Met Ser Ala Gly Phe Trp Gln Pro Gly Pro Gly Gly Pro Pro  
 225 230 235 240  
 Cys Arg Leu Cys Gly Glu Ala Ser Arg Gly Arg Ala Pro Ser Arg Asp  
 245 250 255  
 Glu Gly Ser Leu Leu Leu Gly Ser Arg Arg Pro Arg Arg Asp Ala Ala  
 260 265 270

Glu Arg Cys Ala Ala Ala Leu Met Ala Ser Arg Arg Lys Ser Glu Ala  
 275 280 285  
 Lys Gln Met Pro Arg Ala Ala Pro Ala Thr Arg Val Thr Arg Arg Ser  
 290 295 300  
 Thr Gln Glu Ser Leu Thr Ala Gly Gly Thr Asp Leu Lys Arg Glu Leu  
 305 310 315  
 His Pro Pro Ala Thr Ser His Glu Ala Pro Gly Thr Lys Arg Ser Pro  
 325 330 335  
 Ser Ala Pro Ala Ala Thr Ser Ser Ala Ser Ser Ser Thr Ser Ser Tyr  
 340 345 350  
 Lys Arg Ala Pro Ala Ser Ser Ala Pro Gln Pro Lys Pro Leu Lys Arg  
 355 360 365  
 Phe Lys Arg Ala Ala Gly Lys Lys Gly Ala Arg Thr Arg Gln Gly Pro  
 370 375 380  
 Gly Ala Glu Ser Glu Asp Leu Tyr Asp Phe Val Phe Ile Val Ala Gly  
 385 390 395 400  
 Glu Lys Glu Asp Gly Glu Glu Met Glu Ile Gly Glu Val Ala Cys Gly  
 405 410 415  
 Ala Leu Asp Gly Ser Asp Pro Ser Cys Leu Gly Leu Pro Ala Leu Glu  
 420 425 430  
 Ala Ser Gln Arg Phe Arg Ser Ile Ser Thr Leu Glu Leu Phe Thr Val  
 435 440 445  
 Pro Leu Ser Thr Glu Ala Ala Leu Thr Leu Cys His Leu Leu Ser Ser  
 450 455 460  
 Trp Val Ser Leu Glu Ser Leu Thr Leu Ser Tyr Asn Gly Leu Gly Ser  
 465 470 475 480  
 Asn Ile Phe Arg Leu Leu Asp Ser Leu Arg Ala Leu Ser Gly Gln Ala  
 485 490 495  
 Gly Cys Arg Leu Arg Ala Leu His Leu Ser Asp Leu Phe Ser Pro Leu  
 500 505 510  
 Pro Ile Leu Glu Leu Thr Arg Ala Ile Val Arg Ala Leu Pro Leu Leu  
 515 520 525  
 Arg Val Leu Ser Ile Arg Val Asp His Pro Ser Gln Arg Asp Asn Pro  
 530 535 540  
 Gly Val Pro Gly Asn Ala Gly Pro Pro Ser His Ile Ile Gly Asp Glu  
 545 550 555 560  
 Glu Ile Pro Glu Asn Cys Leu Glu Gln Leu Glu Met Gly Phe Pro Arg  
 565 570 575  
 Gly Ala Gln Pro Ala Pro Leu Leu Cys Ser Val Leu Lys Ala Ser Gly  
 580 585 590  
 Ser Leu Gln Gln Leu Ser Leu Asp Ser Ala Thr Phe Ala Ser Pro Gln  
 595 600 605  
 Asp Phe Gly Leu Val Leu Gln Thr Leu Lys Glu Tyr Asn Leu Ala Leu  
 610 615 620  
 Lys Arg Leu Ser Phe His Asp Met Asn Leu Ala Asp Cys Gln Ser Glu  
 625 630 635 640  
 Val Leu Phe Leu Leu Gln Asn Leu Thr Leu Gln Glu Ile Thr Phe Ser  
 645 650 655  
 Phe Cys Arg Leu Phe Glu Lys Arg Pro Ala Gln Phe Leu Pro Glu Met  
 660 665 670  
 Val Ala Ala Met Lys Gly Asn Ser Thr Leu Lys Gly Leu Arg Leu Pro  
 675 680 685  
 Gly Asn Arg Leu Gly Asn Ala Gly Leu Leu Ala Leu Ala Asp Val Phe  
 690 695 700  
 Ser Glu Asp Ser Ser Ser Ser Leu Cys Gln Leu Asp Ile Ser Ser Asn  
 705 710 715 720  
 Cys Ile Lys Pro Asp Gly Leu Leu Glu Phe Ala Lys Arg Leu Glu Arg  
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 Trp Gly Arg Gly Ala Phe Gly His Leu Arg Leu Phe Gln Asn Trp Leu  
 740 745 750  
 Asp Gln Asp Ala Val Thr Ala Arg Glu Ala Ile Arg Arg Leu Arg Ala  
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 Asp Tyr Val Ser Thr Met  
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<210> 182

<211> 2058

<212> PRT

<213> Homo sapiens

<400> 182

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 Val Phe Arg Thr Asp Tyr Gly Gln Val Phe Thr Tyr Lys Gln Ser Thr  
 35 40 45  
 Ile Thr His Gln Lys Val Thr Ala Met His Pro Thr Asn Glu Glu Gly  
 50 55 60  
 Val Asp Asp Met Ala Ser Leu Thr Glu Leu His Gly Gly Ser Ile Met  
 65 70 75 80  
 Tyr Asn Leu Phe Gln Arg Tyr Lys Arg Asn Gln Ile Tyr Thr Tyr Ile  
 85 90 95  
 Gly Ser Ile Leu Ala Ser Val Asn Pro Tyr Gln Pro Ile Ala Gly Leu  
 100 105 110  
 Tyr Glu Pro Ala Thr Met Glu Gln Tyr Ser Arg Arg His Leu Gly Glu  
 115 120 125  
 Leu Pro Pro His Ile Phe Ala Ile Ala Asn Glu Cys Tyr Arg Cys Leu  
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 Trp Lys Arg Tyr Asp Asn Gln Cys Ile Leu Ile Ser Gly Glu Ser Gly  
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 Ala Gly Lys Thr Glu Ser Thr Lys Leu Ile Leu Lys Phe Leu Ser Val  
 165 170 175  
 Ile Ser Gln Gln Ser Leu Glu Leu Ser Leu Lys Glu Lys Thr Ser Cys  
 180 185 190  
 Val Glu Arg Ala Ile Leu Glu Ser Ser Pro Ile Met Glu Ala Phe Gly  
 195 200 205  
 Asn Ala Lys Thr Val Tyr Asn Asn Asn Ser Ser Arg Phe Gly Lys Phe  
 210 215 220  
 Val Gln Leu Asn Ile Cys Gln Lys Gly Asn Ile Gln Gly Gly Arg Ile  
 225 230 235 240  
 Val Asp Tyr Leu Leu Glu Lys Asn Arg Val Val Arg Gln Asn Pro Gly  
 245 250 255  
 Glu Arg Asn Tyr His Ile Phe Tyr Ala Leu Leu Ala Gly Leu Glu His  
 260 265 270  
 Glu Glu Arg Glu Glu Phe Tyr Leu Ser Thr Pro Glu Asn Tyr His Tyr  
 275 280 285  
 Leu Asn Gln Ser Gly Cys Val Glu Asp Lys Thr Ile Ser Asp Gln Glu  
 290 295 300  
 Ser Phe Arg Glu Val Ile Thr Ala Met Asp Val Met Gln Phe Ser Lys  
 305 310 315 320  
 Glu Glu Val Arg Glu Val Ser Arg Leu Leu Ala Gly Ile Leu His Leu  
 325 330 335  
 Gly Asn Ile Glu Phe Ile Thr Ala Gly Gly Ala Gln Val Ser Phe Lys  
 340 345 350  
 Thr Ala Leu Gly Arg Ser Ala Glu Leu Leu Gly Leu Asp Pro Thr Gln  
 355 360 365

Leu Thr Asp Ala Leu Thr Gln Arg Ser Met Phe Leu Arg Gly Glu Glu  
 370 375 380  
 Ile Leu Thr Pro Leu Asn Val Gln Gln Ala Val Asp Ser Arg Asp Ser  
 385 390 395 400  
 Leu Ala Met Ala Leu Tyr Ala Cys Cys Phe Glu Trp Val Ile Lys Lys  
 405 410 415  
 Ile Asn Ser Arg Ile Lys Gly Asn Glu Asp Phe Lys Ser Ile Gly Ile  
 420 425 430  
 Leu Asp Ile Phe Gly Phe Glu Asn Phe Glu Val Asn His Phe Glu Gln  
 435 440 445  
 Phe Asn Ile Asn Tyr Ala Asn Glu Lys Leu Gln Glu Tyr Phe Asn Lys  
 450 455 460  
 His Ile Phe Ser Leu Glu Gln Leu Glu Tyr Ser Arg Glu Gly Leu Val  
 465 470 475 480  
 Trp Glu Asp Ile Asp Trp Ile Asp Asn Gly Glu Cys Leu Asp Leu Ile  
 485 490 495  
 Glu Lys Lys Leu Gly Leu Leu Ala Leu Ile Asn Glu Glu Ser His Phe  
 500 505 510  
 Pro Gln Ala Thr Asp Ser Thr Leu Leu Glu Lys Leu His Ser Gln His  
 515 520 525  
 Ala Asn Asn His Phe Tyr Val Lys Pro Arg Val Ala Val Asn Asn Phe  
 530 535 540  
 Gly Val Lys His Tyr Ala Gly Glu Val Gln Tyr Asp Val Arg Gly Ile  
 545 550 555 560  
 Leu Glu Lys Asn Arg Asp Thr Phe Arg Asp Asp Leu Leu Asn Leu Leu  
 565 570 575  
 Arg Glu Ser Arg Phe Asp Phe Ile Tyr Asp Leu Phe Glu His Val Ser  
 580 585 590  
 Ser Arg Asn Asn Gln Asp Thr Leu Lys Cys Gly Ser Lys His Arg Arg  
 595 600 605  
 Pro Thr Val Ser Ser Gln Phe Lys Asp Ser Leu His Ser Leu Met Ala  
 610 615 620  
 Thr Leu Ser Ser Ser Asn Pro Phe Phe Val Arg Cys Ile Lys Pro Asn  
 625 630 635 640  
 Met Gln Lys Met Pro Asp Gln Phe Asp Gln Ala Val Val Leu Asn Gln  
 645 650 655  
 Leu Arg Tyr Ser Gly Met Leu Glu Thr Val Arg Ile Arg Lys Ala Gly  
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 Tyr Ala Val Arg Arg Pro Phe Gln Asp Phe Tyr Lys Arg Tyr Lys Val  
 675 680 685  
 Leu Met Arg Asn Leu Ala Leu Pro Glu Asp Val Arg Gly Lys Cys Thr  
 690 695 700  
 Ser Leu Leu Gln Leu Tyr Asp Ala Ser Asn Ser Glu Trp Gln Leu Gly  
 705 710 715 720  
 Lys Thr Lys Val Phe Leu Arg Glu Ser Leu Glu Gln Lys Leu Glu Lys  
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 Arg Arg Glu Glu Glu Val Ser His Ala Ala Met Val Ile Arg Ala His  
 740 745 750  
 Val Leu Gly Phe Leu Ala Arg Lys Gln Tyr Arg Lys Val Leu Tyr Cys  
 755 760 765  
 Val Val Ile Ile Gln Lys Asn Tyr Arg Ala Phe Leu Leu Arg Arg Arg  
 770 775 780  
 Phe Leu His Leu Lys Lys Ala Ala Ile Val Phe Gln Lys Gln Leu Arg  
 785 790 795 800  
 Gly Gln Ile Ala Arg Arg Val Tyr Arg Gln Leu Leu Ala Glu Lys Arg  
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 820 825 830  
 Glu Glu Glu Glu Arg Glu Arg Glu Arg Glu Arg Arg Glu Ala Glu Leu  
 835 840 845  
 Arg Ala Gln Gln Glu Glu Glu Thr Arg Lys Gln Gln Glu Leu Glu Ala  
 850 855 860

Leu Gln Lys Ser Gln Lys Glu Ala Glu Leu Thr Arg Glu Leu Glu Lys  
 865 870 875 880  
 Gln Lys Glu Asn Lys Gln Val Glu Glu Ile Leu Arg Leu Glu Lys Glu  
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 Ile Glu Asp Leu Gln Arg Met Lys Glu Gln Gln Glu Leu Ser Leu Thr  
 900 905 910  
 Glu Ala Ser Leu Gln Lys Leu Gln Glu Arg Arg Asp Gln Glu Leu Arg  
 915 920 925  
 Arg Leu Glu Glu Glu Ala Cys Arg Ala Ala Gln Glu Phe Leu Glu Ser  
 930 935 940  
 Leu Asn Phe Asp Glu Ile Asp Glu Cys Val Arg Asn Ile Glu Arg Ser  
 945 950 955 960  
 Leu Ser Val Gly Ser Glu Phe Ser Ser Glu Leu Ala Glu Ser Ala Cys  
 965 970 975  
 Glu Glu Lys Pro Asn Phe Asn Phe Ser Gln Pro Tyr Pro Glu Glu Glu  
 980 985 990  
 Val Asp Glu Gly Phe Glu Ala Asp Asp Ala Phe Lys Asp Ser Pro  
 995 1000 1005  
 Asn Pro Ser Glu His Gly His Ser Asp Gln Arg Thr Ser Gly Ile  
 1010 1015 1020  
 Arg Thr Ser Asp Asp Ser Ser Glu Glu Asp Pro Tyr Met Asn Asp  
 1025 1030 1035  
 Thr Val Val Pro Thr Ser Pro Ser Ala Asp Ser Thr Val Leu Leu  
 1040 1045 1050  
 Ala Pro Ser Val Gln Asp Ser Gly Ser Leu His Asn Ser Ser Ser  
 1055 1060 1065  
 Gly Glu Ser Thr Tyr Cys Met Pro Gln Asn Ala Gly Asp Leu Pro  
 1070 1075 1080  
 Ser Pro Asp Gly Asp Tyr Asp Tyr Asp Gln Asp Asp Tyr Glu Asp  
 1085 1090 1095  
 Gly Ala Ile Thr Ser Gly Ser Ser Val Thr Phe Ser Asn Ser Tyr  
 1100 1105 1110  
 Gly Ser Gln Trp Ser Pro Asp Tyr Arg Cys Ser Val Gly Thr Tyr  
 1115 1120 1125  
 Asn Ser Ser Gly Ala Tyr Arg Phe Ser Ser Glu Gly Ala Gln Ser  
 1130 1135 1140  
 Ser Phe Glu Asp Ser Glu Glu Asp Phe Asp Ser Arg Phe Asp Thr  
 1145 1150 1155  
 Asp Asp Glu Leu Ser Tyr Arg Arg Asp Ser Val Tyr Ser Cys Val  
 1160 1165 1170  
 Thr Leu Pro Tyr Phe His Ser Phe Leu Tyr Met Lys Gly Gly Leu  
 1175 1180 1185  
 Met Asn Ser Trp Lys Arg Arg Trp Cys Val Leu Lys Asp Glu Thr  
 1190 1195 1200  
 Phe Leu Trp Phe Arg Ser Lys Gln Glu Ala Leu Lys Gln Gly Trp  
 1205 1210 1215  
 Leu His Lys Lys Gly Gly Gly Ser Ser Thr Leu Ser Arg Arg Asn  
 1220 1225 1230  
 Trp Lys Lys Arg Trp Phe Val Leu Arg Gln Ser Lys Leu Met Tyr  
 1235 1240 1245  
 Phe Glu Asn Asp Ser Glu Glu Lys Leu Lys Gly Thr Val Glu Val  
 1250 1255 1260  
 Arg Thr Ala Lys Glu Ile Ile Asp Asn Thr Thr Lys Glu Asn Gly  
 1265 1270 1275  
 Ile Asp Ile Ile Met Ala Asp Arg Thr Phe His Leu Ile Ala Glu  
 1280 1285 1290  
 Ser Pro Glu Asp Ala Ser Gln Trp Phe Ser Val Leu Ser Gln Val  
 1295 1300 1305  
 His Ala Ser Thr Asp Gln Glu Ile Gln Glu Met His Asp Glu Gln  
 1310 1315 1320  
 Ala Asn Pro Gln Asn Ala Val Gly Thr Leu Asp Val Gly Leu Ile  
 1325 1330 1335

Asp	Ser	Val	Cys	Ala	Ser	Asp	Ser	Pro	Asp	Arg	Pro	Asn	Ser	Phe
1340						1345					1350			
Val	Ile	Ile	Thr	Ala	Asn	Arg	Val	Leu	His	Cys	Asn	Ala	Asp	Thr
1355						1360					1365			
Pro	Glu	Glu	Met	His	His	Trp	Ile	Thr	Leu	Leu	Gln	Arg	Ser	Lys
1370						1375					1380			
Gly	Asp	Thr	Arg	Val	Glu	Gly	Gln	Glu	Phe	Ile	Val	Arg	Gly	Trp
1385						1390					1395			
Leu	His	Lys	Glu	Val	Lys	Asn	Ser	Pro	Lys	Met	Ser	Ser	Leu	Lys
1400						1405					1410			
Leu	Lys	Lys	Arg	Trp	Phe	Val	Leu	Thr	His	Asn	Ser	Leu	Asp	Tyr
1415						1420					1425			
Tyr	Lys	Ser	Ser	Glu	Lys	Asn	Ala	Leu	Lys	Leu	Gly	Thr	Leu	Val
1430						1435					1440			
Leu	Asn	Ser	Leu	Cys	Ser	Val	Val	Pro	Pro	Asp	Glu	Lys	Ile	Phe
1445						1450					1455			
Lys	Glu	Thr	Gly	Tyr	Trp	Asn	Val	Thr	Val	Tyr	Gly	Arg	Lys	His
1460						1465					1470			
Cys	Tyr	Arg	Leu	Tyr	Thr	Lys	Leu	Leu	Asn	Glu	Ala	Thr	Arg	Trp
1475						1480					1485			
Ser	Ser	Ala	Ile	Gln	Asn	Val	Thr	Asp	Thr	Lys	Ala	Pro	Ile	Asp
1490						1495					1500			
Thr	Pro	Thr	Gln	Gln	Leu	Ile	Gln	Asp	Ile	Lys	Glu	Asn	Cys	Leu
1505						1510					1515			
Asn	Ser	Asp	Val	Val	Glu	Gln	Ile	Tyr	Lys	Arg	Asn	Pro	Ile	Leu
1520						1525					1530			
Arg	Tyr	Thr	His	His	Pro	Leu	His	Ser	Pro	Leu	Leu	Pro	Leu	Pro
1535						1540					1545			
Tyr	Gly	Asp	Ile	Asn	Leu	Asn	Leu	Leu	Lys	Asp	Lys	Gly	Tyr	Thr
1550						1555					1560			
Thr	Leu	Gln	Asp	Glu	Ala	Ile	Lys	Ile	Phe	Asn	Ser	Leu	Gln	Gln
1565						1570					1575			
Leu	Glu	Ser	Met	Ser	Asp	Pro	Ile	Pro	Ile	Ile	Gln	Gly	Ile	Leu
1580						1585					1590			
Gln	Thr	Gly	His	Asp	Leu	Arg	Pro	Leu	Arg	Asp	Glu	Leu	Tyr	Cys
1595						1600					1605			
Gln	Leu	Ile	Lys	Gln	Thr	Asn	Lys	Val	Pro	His	Pro	Gly	Ser	Val
1610						1615					1620			
Gly	Asn	Leu	Tyr	Ser	Trp	Gln	Ile	Leu	Thr	Cys	Leu	Ser	Cys	Thr
1625						1630					1635			
Phe	Leu	Pro	Ser	Arg	Gly	Ile	Leu	Lys	Tyr	Leu	Lys	Phe	His	Leu
1640						1645					1650			
Lys	Arg	Ile	Arg	Glu	Gln	Phe	Pro	Gly	Thr	Glu	Met	Glu	Lys	Tyr
1655						1660					1665			
Ala	Leu	Phe	Thr	Tyr	Glu	Ser	Leu	Lys	Lys	Thr	Lys	Cys	Arg	Glu
1670						1675					1680			
Phe	Val	Pro	Ser	Arg	Asp	Glu	Ile	Glu	Ala	Leu	Ile	His	Arg	Gln
1685						1690					1695			
Glu	Met	Thr	Ser	Thr	Val	Tyr	Cys	His	Gly	Gly	Gly	Ser	Cys	Lys
1700						1705					1710			
Ile	Thr	Ile	Asn	Ser	His	Thr	Thr	Ala	Gly	Glu	Val	Val	Glu	Lys
1715						1720					1725			
Leu	Ile	Arg	Gly	Leu	Ala	Met	Glu	Asp	Ser	Arg	Asn	Met	Phe	Ala
1730						1735					1740			
Leu	Phe	Glu	Tyr	Asn	Gly	His	Val	Asp	Lys	Ala	Ile	Glu	Ser	Arg
1745						1750					1755			
Thr	Val	Val	Ala	Asp	Val	Leu	Ala	Lys	Phe	Glu	Lys	Leu	Ala	Ala
1760						1765					1770			
Thr	Ser	Glu	Val	Gly	Asp	Leu	Pro	Trp	Lys	Phe	Tyr	Phe	Lys	Leu
1775						1780					1785			
Tyr	Cys	Phe	Leu	Asp	Thr	Asp	Asn	Val	Pro	Lys	Asp	Ser	Val	Glu
1790						1795					1800			

Phe	Ala	Phe	Met	Phe	Glu	Gln	Ala	His	Glu	Ala	Val	Ile	His	Gly
1805						1810					1815			
His	His	Pro	Ala	Pro	Glu	Glu	Asn	Leu	Gln	Val	Leu	Ala	Ala	Leu
1820						1825					1830			
Arg	Leu	Gln	Tyr	Leu	Gln	Gly	Asp	Tyr	Thr	Leu	His	Ala	Ala	Ile
1835						1840					1845			
Pro	Pro	Leu	Glu	Glu	Val	Tyr	Ser	Leu	Gln	Arg	Leu	Lys	Ala	Arg
1850						1855					1860			
Ile	Ser	Gln	Ser	Thr	Lys	Thr	Phe	Thr	Pro	Cys	Glu	Arg	Leu	Glu
1865						1870					1875			
Lys	Arg	Arg	Thr	Ser	Phe	Leu	Glu	Gly	Thr	Leu	Arg	Arg	Ser	Phe
1880						1885					1890			
Arg	Thr	Gly	Ser	Val	Val	Arg	Gln	Lys	Val	Glu	Glu	Glu	Gln	Met
1895						1900					1905			
Leu	Asp	Met	Trp	Ile	Lys	Glu	Glu	Val	Ser	Ser	Ala	Arg	Ala	Ser
1910						1915					1920			
Ile	Ile	Asp	Lys	Trp	Arg	Lys	Phe	Gln	Gly	Met	Asn	Gln	Glu	Gln
1925						1930					1935			
Ala	Met	Ala	Lys	Tyr	Met	Ala	Leu	Ile	Lys	Glu	Trp	Pro	Gly	Tyr
1940						1945					1950			
Gly	Ser	Thr	Leu	Phe	Asp	Val	Glu	Cys	Lys	Glu	Gly	Gly	Phe	Pro
1955						1960					1965			
Gln	Glu	Leu	Trp	Leu	Gly	Val	Ser	Ala	Asp	Ala	Val	Ser	Val	Tyr
1970						1975					1980			
Lys	Arg	Gly	Glu	Gly	Arg	Pro	Leu	Glu	Val	Phe	Gln	Tyr	Glu	His
1985						1990					1995			
Ile	Leu	Ser	Phe	Gly	Ala	Pro	Leu	Ala	Asn	Thr	Tyr	Lys	Ile	Val
2000						2005					2010			
Val	Asp	Glu	Arg	Glu	Leu	Leu	Phe	Glu	Thr	Ser	Glu	Val	Val	Asp
2015						2020					2025			
Val	Ala	Lys	Leu	Met	Lys	Ala	Tyr	Ile	Ser	Met	Ile	Val	Lys	Lys
2030						2035					2040			
Arg	Tyr	Ser	Thr	Thr	Arg	Ser	Ala	Ser	Ser	Gln	Gly	Ser	Ser	Arg
2045						2050					2055			

&lt;210&gt; 183

&lt;211&gt; 1210

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 183

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Ala	Leu	Cys	Pro	Ala	Ser	Arg	Ala	Leu	Glu	Glu	Lys	Lys	Val	Cys	Gln
			20				25						30		
Gly	Thr	Ser	Asn	Lys	Leu	Thr	Gln	Leu	Gly	Thr	Phe	Glu	Asp	His	Phe
			35				40					45			
Leu	Ser	Leu	Gln	Arg	Met	Phe	Asn	Asn	Cys	Glu	Val	Val	Leu	Gly	Asn
			50			55					60				
Leu	Glu	Ile	Thr	Tyr	Val	Gln	Arg	Asn	Tyr	Asp	Leu	Ser	Phe	Leu	Lys
65				70					75					80	
Thr	Ile	Gln	Glu	Val	Ala	Gly	Tyr	Val	Leu	Ile	Ala	Leu	Asn	Thr	Val
				85					90				95		
Glu	Arg	Ile	Pro	Leu	Glu	Asn	Leu	Gln	Ile	Ile	Arg	Gly	Asn	Met	Tyr
			100					105					110		
Tyr	Glu	Asn	Ser	Tyr	Ala	Leu	Ala	Val	Leu	Ser	Asn	Tyr	Asp	Ala	Asn
			115				120						125		

Lys	Thr	Gly	Leu	Lys	Glu	Leu	Pro	Met	Arg	Asn	Leu	Gln	Glu	Ile	Leu
	130					135					140				
His	Gly	Ala	Val	Arg	Phe	Ser	Asn	Asn	Pro	Ala	Leu	Cys	Asn	Val	Glu
145					150					155					160
Ser	Ile	Gln	Trp	Arg	Asp	Ile	Val	Ser	Ser	Asp	Phe	Leu	Ser	Asn	Met
				165					170					175	
Ser	Met	Asp	Phe	Gln	Asn	His	Leu	Gly	Ser	Cys	Gln	Lys	Cys	Asp	Pro
			180					185					190		
Ser	Cys	Pro	Asn	Gly	Ser	Cys	Trp	Gly	Ala	Gly	Glu	Glu	Asn	Cys	Gln
		195					200					205			
Lys	Leu	Thr	Lys	Ile	Ile	Cys	Ala	Gln	Gln	Cys	Ser	Gly	Arg	Cys	Arg
	210					215					220				
Gly	Lys	Ser	Pro	Ser	Asp	Cys	Cys	His	Asn	Gln	Cys	Ala	Ala	Gly	Cys
225					230					235					240
Thr	Gly	Pro	Arg	Glu	Ser	Asp	Cys	Leu	Val	Cys	Arg	Lys	Phe	Arg	Asp
				245					250					255	
Glu	Ala	Thr	Cys	Lys	Asp	Thr	Cys	Pro	Pro	Leu	Met	Leu	Tyr	Asn	Pro
			260					265					270		
Thr	Thr	Tyr	Gln	Met	Asp	Val	Asn	Pro	Glu	Gly	Lys	Tyr	Ser	Phe	Gly
		275					280					285			
Ala	Thr	Cys	Val	Lys	Lys	Cys	Pro	Arg	Asn	Tyr	Val	Val	Thr	Asp	His
	290					295					300				
Gly	Ser	Cys	Val	Arg	Ala	Cys	Gly	Ala	Asp	Ser	Tyr	Glu	Met	Glu	Glu
305					310				315						320
Asp	Gly	Val	Arg	Lys	Cys	Lys	Lys	Cys	Glu	Gly	Pro	Cys	Arg	Lys	Val
				325					330					335	
Cys	Asn	Gly	Ile	Gly	Ile	Gly	Glu	Phe	Lys	Asp	Ser	Leu	Ser	Ile	Asn
			340					345					350		
Ala	Thr	Asn	Ile	Lys	His	Phe	Lys	Asn	Cys	Thr	Ser	Ile	Ser	Gly	Asp
		355					360					365			
Leu	His	Ile	Leu	Pro	Val	Ala	Phe	Arg	Gly	Asp	Ser	Phe	Thr	His	Thr
	370					375					380				
Pro	Pro	Leu	Asp	Pro	Gln	Glu	Leu	Asp	Ile	Leu	Lys	Thr	Val	Lys	Glu
385					390					395					400
Ile	Thr	Gly	Phe	Leu	Leu	Ile	Gln	Ala	Trp	Pro	Glu	Asn	Arg	Thr	Asp
			405						410					415	
Leu	His	Ala	Phe	Glu	Asn	Leu	Glu	Ile	Arg	Gly	Arg	Thr	Lys	Gln	
			420					425				430			
His	Gly	Gln	Phe	Ser	Leu	Ala	Val	Val	Ser	Leu	Asn	Ile	Thr	Ser	Leu
		435					440					445			
Gly	Leu	Arg	Ser	Leu	Lys	Glu	Ile	Ser	Asp	Gly	Asp	Val	Ile	Ile	Ser
	450					455					460				
Gly	Asn	Lys	Asn	Leu	Cys	Tyr	Ala	Asn	Thr	Ile	Asn	Trp	Lys	Lys	Leu
465					470					475					480
Phe	Gly	Thr	Ser	Gly	Gln	Lys	Thr	Lys	Ile	Ile	Ser	Asn	Arg	Gly	Glu
				485					490					495	
Asn	Ser	Cys	Lys	Ala	Thr	Gly	Gln	Val	Cys	His	Ala	Leu	Cys	Ser	Pro
			500					505					510		
Glu	Gly	Cys	Trp	Gly	Pro	Glu	Pro	Arg	Asp	Cys	Val	Ser	Cys	Arg	Asn
		515					520					525			
Val	Ser	Arg	Gly	Arg	Glu	Cys	Val	Asp	Lys	Cys	Asn	Leu	Leu	Glu	Gly
		530				535					540				
Glu	Pro	Arg	Glu	Phe	Val	Glu	Asn	Ser	Glu	Cys	Ile	Gln	Cys	His	Pro
				550						555					560
Glu	Cys	Leu	Pro	Gln	Ala	Met	Asn	Ile	Thr	Cys	Thr	Gly	Arg	Gly	Pro
				565					570					575	
Asp	Asn	Cys	Ile	Gln	Cys	Ala	His	Tyr	Ile	Asp	Gly	Pro	His	Cys	Val
			580					585					590		
Lys	Thr	Cys	Pro	Ala	Gly	Val	Met	Gly	Glu	Asn	Asn	Thr	Leu	Val	Trp
		595					600					605			
Lys	Tyr	Ala	Asp	Ala	Gly	His	Val	Cys	His	Leu	Cys	His	Pro	Asn	Cys
	610					615					620				

Thr Tyr Gly Cys Thr Gly Pro Gly Leu Glu Gly Cys Pro Thr Asn Gly  
 625 630 635 640  
 Pro Lys Ile Pro Ser Ile Ala Thr Gly Met Val Gly Ala Leu Leu Leu  
 645 650 655  
 Leu Leu Val Val Ala Leu Gly Ile Gly Leu Phe Met Arg Arg Arg His  
 660 665 670  
 Ile Val Arg Lys Arg Thr Leu Arg Arg Leu Leu Gln Glu Arg Glu Leu  
 675 680 685  
 Val Glu Pro Leu Thr Pro Ser Gly Glu Ala Pro Asn Gln Ala Leu Leu  
 690 695 700  
 Arg Ile Leu Lys Glu Thr Glu Phe Lys Lys Ile Lys Val Leu Gly Ser  
 705 710 715 720  
 Gly Ala Phe Gly Thr Val Tyr Lys Gly Leu Trp Ile Pro Glu Gly Glu  
 725 730 735  
 Lys Val Lys Ile Pro Val Ala Ile Lys Glu Leu Arg Glu Ala Thr Ser  
 740 745 750  
 Pro Lys Ala Asn Lys Glu Ile Leu Asp Glu Ala Tyr Val Met Ala Ser  
 755 760 765  
 Val Asp Asn Pro His Val Cys Arg Leu Leu Gly Ile Cys Leu Thr Ser  
 770 775 780  
 Thr Val Gln Leu Ile Thr Gln Leu Met Pro Phe Gly Cys Leu Leu Asp  
 785 790 795 800  
 Tyr Val Arg Glu His Lys Asp Asn Ile Gly Ser Gln Tyr Leu Leu Asn  
 805 810 815  
 Trp Cys Val Gln Ile Ala Lys Gly Met Asn Tyr Leu Glu Asp Arg Arg  
 820 825 830  
 Leu Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Lys Thr Pro  
 835 840 845  
 Gln His Val Lys Ile Thr Asp Phe Gly Leu Ala Lys Leu Leu Gly Ala  
 850 855 860  
 Glu Glu Lys Glu Tyr His Ala Glu Gly Gly Lys Val Pro Ile Lys Trp  
 865 870 875 880  
 Met Ala Leu Glu Ser Ile Leu His Arg Ile Tyr Thr His Gln Ser Asp  
 885 890 895  
 Val Trp Ser Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ser  
 900 905 910  
 Lys Pro Tyr Asp Gly Ile Pro Ala Ser Glu Ile Ser Ser Ile Leu Glu  
 915 920 925  
 Lys Gly Glu Arg Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr  
 930 935 940  
 Met Ile Met Val Lys Cys Trp Met Ile Asp Ala Asp Ser Arg Pro Lys  
 945 950 955 960  
 Phe Arg Glu Leu Ile Glu Phe Ser Lys Met Ala Arg Asp Pro Gln  
 965 970 975  
 Arg Tyr Leu Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro  
 980 985 990  
 Thr Asp Ser Asn Phe Tyr Arg Ala Leu Met Asp Glu Glu Asp Met Asp  
 995 1000 1005  
 Asp Val Val Asp Ala Asp Glu Tyr Leu Ile Pro Gln Gln Gly Phe  
 1010 1015 1020  
 Phe Ser Ser Pro Ser Thr Ser Arg Thr Pro Leu Leu Ser Ser Leu  
 1025 1030 1035  
 Ser Ala Thr Ser Asn Asn Ser Thr Val Ala Cys Ile Asp Arg Asn  
 1040 1045 1050  
 Gly Leu Gln Ser Cys Pro Ile Lys Glu Asp Ser Phe Leu Gln Arg  
 1055 1060 1065  
 Tyr Ser Ser Asp Pro Thr Gly Ala Leu Thr Glu Asp Ser Ile Asp  
 1070 1075 1080  
 Asp Thr Phe Leu Pro Val Pro Glu Tyr Ile Asn Gln Ser Val Pro  
 1085 1090 1095  
 Lys Arg Pro Ala Gly Ser Val Gln Asn Pro Val Tyr His Asn Gln  
 1100 1105 1110

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Pro Leu Asn Pro Ala Pro Ser Arg Asp Pro His Tyr Gln Asp Pro  
 1115 1120 1125  
 His Ser Thr Ala Val Gly Asn Pro Glu Tyr Leu Asn Thr Val Gln  
 1130 1135 1140  
 Pro Thr Cys Val Asn Ser Thr Phe Asp Ser Pro Ala His Trp Ala  
 1145 1150 1155  
 Gln Lys Gly Ser His Gln Ile Ser Leu Asp Asn Pro Asp Tyr Gln  
 1160 1165 1170  
 Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro Asn Gly Ile Phe Lys  
 1175 1180 1185  
 Gly Ser Thr Ala Glu Asn Ala Glu Tyr Leu Arg Val Ala Pro Gln  
 1190 1195 1200  
 Ser Ser Glu Phe Ile Gly Ala  
 1205 1210

&lt;210&gt; 184

&lt;211&gt; 453

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 184

Met Pro Lys Asn Lys Lys Arg Asn Thr Pro His Arg Gly Ser Ser Ala  
 1 5 10 15  
 Gly Gly Gly Gly Ser Gly Ala Ala Ala Thr Ala Ala Thr Ala Gly  
 20 25 30  
 Gly Gln His Arg Asn Val Gln Pro Phe Ser Asp Glu Asp Ala Ser Ile  
 35 40 45  
 Glu Thr Met Ser His Cys Ser Gly Tyr Ser Asp Pro Ser Ser Phe Ala  
 50 55 60  
 Glu Asp Gly Pro Glu Val Leu Asp Glu Glu Gly Thr Gln Glu Asp Leu  
 65 70 75 80  
 Glu Tyr Lys Arg Lys Gly Leu Ile Asp Leu Thr Leu Asp Lys Ser Ala  
 85 90 95  
 Lys Thr Arg Gln Ala Ala Leu Glu Gly Ile Lys Asn Ala Leu Ala Ser  
 100 105 110  
 Lys Met Leu Tyr Glu Phe Ile Leu Glu Arg Arg Met Thr Leu Thr Asp  
 115 120 125  
 Ser Ile Glu Arg Cys Leu Lys Lys Gly Lys Ser Asp Glu Gln Arg Ala  
 130 135 140  
 Ala Ala Ala Leu Ala Ser Val Leu Cys Ile Gln Leu Gly Pro Gly Ile  
 145 150 155 160  
 Glu Ser Glu Glu Ile Leu Lys Thr Leu Gly Pro Ile Leu Lys Lys Ile  
 165 170 175  
 Ile Cys Asp Gly Ser Ala Ser Met Gln Ala Arg Gln Thr Cys Ala Thr  
 180 185 190  
 Cys Phe Gly Val Cys Cys Phe Ile Ala Thr Asp Asp Ile Thr Glu Leu  
 195 200 205  
 Tyr Ser Thr Leu Glu Cys Leu Glu Asn Ile Phe Thr Lys Ser Tyr Leu  
 210 215 220  
 Lys Glu Lys Asp Thr Thr Val Ile Cys Ser Thr Pro Asn Thr Val Leu  
 225 230 235 240  
 His Ile Ser Ser Leu Leu Ala Trp Thr Leu Leu Thr Ile Cys Pro  
 245 250 255  
 Ile Asn Glu Val Lys Lys Lys Leu Glu Met His Phe His Lys Leu Pro  
 260 265 270  
 Ser Leu Leu Ser Cys Asp Asp Val Asn Met Arg Ile Ala Ala Gly Glu  
 275 280 285



Ser Leu Ala Leu Leu Phe Glu Leu Ala Arg Gly Ile Glu Ser Asp Phe  
 290 295 300  
 Phe Tyr Glu Asp Met Glu Ser Leu Thr Gln Met Leu Arg Ala Leu Ala  
 305 310 315 320  
 Thr Asp Gly Asn Lys His Arg Ala Lys Val Asp Lys Arg Lys Gln Arg  
 325 330 335  
 Ser Val Phe Arg Asp Val Leu Arg Ala Val Glu Glu Arg Asp Phe Pro  
 340 345 350  
 Thr Glu Thr Ile Lys Phe Gly Pro Glu Arg Met Tyr Ile Asp Cys Trp  
 355 360 365  
 Val Lys Lys His Thr Tyr Asp Thr Phe Lys Glu Val Leu Gly Ser Gly  
 370 375 380  
 Met Gln Tyr Pro Leu Ala Val Lys Met Glu Phe Leu Glu Asn Val Phe  
 385 390 395 400  
 Glu Thr Trp Thr Pro Ser Asp Ala Leu Met Leu Gln Arg Leu Lys Thr  
 405 410 415  
 Met Lys Ile Ser Arg Phe Glu Arg His Leu Tyr Asn Ser Ala Ala Phe  
 420 425 430  
 Lys Ala Arg Thr Lys Ala Arg Ser Lys Cys Arg Asp Lys Arg Ala Asp  
 435 440 445  
 Val Gly Glu Phe Phe  
 450

&lt;210&gt; 185

&lt;211&gt; 341

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 185

Met Pro Lys Arg Lys Val Thr Phe Gln Gly Val Gly Asp Glu Glu Asp  
 1 5 10 15  
 Glu Asp Glu Ile Ile Val Pro Lys Lys Lys Leu Val Asp Pro Val Ala  
 20 25 30  
 Gly Ser Gly Gly Pro Gly Ser Arg Phe Lys Gly Lys His Ser Leu Asp  
 35 40 45  
 Ser Asp Glu Glu Glu Asp Asp Asp Asp Gly Gly Ser Ser Lys Tyr Asp  
 50 55 60  
 Ile Leu Ala Ser Glu Asp Val Glu Gly Gln Glu Ala Ala Thr Leu Pro  
 65 70 75 80  
 Ser Glu Gly Gly Val Arg Ile Thr Pro Phe Asn Leu Gln Glu Glu Met  
 85 90 95  
 Glu Glu Gly His Phe Asp Ala Asp Gly Asn Tyr Phe Leu Asn Arg Asp  
 100 105 110  
 Ala Gln Ile Arg Asp Ser Trp Leu Asp Asn Ile Asp Trp Val Lys Ile  
 115 120 125  
 Arg Glu Arg Pro Pro Gly Gln Arg Gln Ala Ser Asp Ser Glu Glu Glu  
 130 135 140  
 Asp Ser Leu Gly Gln Thr Ser Met Ser Ala Gln Ala Leu Leu Glu Gly  
 145 150 155 160  
 Leu Leu Glu Leu Leu Leu Pro Arg Glu Thr Val Ala Gly Ala Leu Arg  
 165 170 175  
 Arg Leu Gly Ala Arg Gly Gly Gly Lys Gly Arg Lys Gly Pro Gly Gln  
 180 185 190  
 Pro Ser Ser Pro Gln Arg Leu Asp Arg Leu Ser Gly Leu Ala Asp Gln  
 195 200 205  
 Met Val Ala Arg Gly Asn Leu Gly Val Tyr Gln Glu Thr Arg Glu Arg  
 210 215 220

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Leu Ala Met Arg Leu Lys Gly Leu Gly Cys Gln Thr Leu Gly Pro His  
 225 230 235 240  
 Asn Pro Thr Pro Pro Ser Leu Asp Met Phe Ala Glu Glu Leu Ala  
 245 250 255  
 Glu Glu Glu Leu Glu Thr Pro Thr Pro Thr Gln Arg Gly Glu Ala Glu  
 260 265 270  
 Ser Arg Gly Asp Gly Leu Val Asp Val Met Trp Glu Tyr Lys Trp Glu  
 275 280 285  
 Asn Thr Gly Asp Ala Glu Leu Tyr Gly Pro Phe Thr Ser Ala Gln Met  
 290 295 300  
 Gln Thr Trp Val Ser Glu Gly Tyr Phe Pro Asp Gly Val Tyr Cys Arg  
 305 310 315 320  
 Lys Leu Asp Pro Pro Gly Gly Gln Phe Tyr Asn Ser Lys Arg Ile Asp  
 325 330 335  
 Phe Asp Leu Tyr Thr  
 340

&lt;210&gt; 186

&lt;211&gt; 182

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 186

Met Gly Leu Leu Ser Ile Leu Arg Lys Leu Lys Ser Ala Pro Asp Gln  
 1 5 10 15  
 Glu Val Arg Ile Leu Leu Leu Gly Leu Asp Asn Ala Gly Lys Thr Thr  
 20 25 30  
 Leu Leu Lys Gln Leu Ala Ser Glu Asp Ile Ser His Ile Thr Pro Thr  
 35 40 45  
 Gln Gly Phe Asn Ile Lys Ser Val Gln Ser Gln Gly Phe Lys Leu Asn  
 50 55 60  
 Val Trp Asp Ile Gly Gly Gln Arg Lys Ile Arg Pro Tyr Trp Lys Asn  
 65 70 75 80  
 Tyr Phe Glu Asn Thr Asp Ile Leu Ile Tyr Val Ile Asp Ser Ala Asp  
 85 90 95  
 Arg Lys Arg Phe Glu Glu Thr Gly Gln Glu Leu Ala Glu Leu Leu Glu  
 100 105 110  
 Glu Glu Lys Leu Ser Cys Val Pro Val Leu Ile Phe Ala Asn Lys Gln  
 115 120 125  
 Asp Leu Leu Thr Ala Ala Pro Ala Ser Glu Ile Ala Glu Gly Leu Asn  
 130 135 140  
 Leu His Thr Ile Arg Asp Arg Val Trp Gln Ile Gln Ser Cys Ser Ala  
 145 150 155 160  
 Leu Thr Gly Glu Gly Val Gln Asp Gly Met Asn Trp Val Cys Lys Asn  
 165 170 175  
 Val Asn Ala Lys Lys Lys  
 180

&lt;210&gt; 187

&lt;211&gt; 398

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 187  
 Met Ala Leu Leu Arg Arg Pro Thr Val Ser Ser Asp Leu Glu Asn Ile  
 1 5 10 15  
 Asp Thr Gly Val Asn Ser Lys Val Lys Ser His Val Thr Ile Arg Arg  
 20 25 30  
 Thr Val Leu Glu Glu Ile Gly Asn Arg Val Thr Thr Arg Ala Ala Gln  
 35 40 45  
 Val Ala Lys Lys Ala Gln Asn Thr Lys Val Pro Val Gln Pro Thr Lys  
 50 55 60  
 Thr Thr Asn Val Asn Lys Gln Leu Lys Pro Thr Ala Ser Val Lys Pro  
 65 70 75 80  
 Val Gln Met Glu Lys Leu Ala Pro Lys Gly Pro Ser Pro Thr Pro Glu  
 85 90 95  
 Asp Val Ser Met Lys Glu Glu Asn Leu Cys Gln Ala Phe Ser Asp Ala  
 100 105 110  
 Leu Leu Cys Lys Ile Glu Asp Ile Asp Asn Glu Asp Trp Glu Asn Pro  
 115 120 125  
 Gln Leu Cys Ser Asp Tyr Val Lys Asp Ile Tyr Gln Tyr Leu Arg Gln  
 130 135 140  
 Leu Glu Val Leu Gln Ser Ile Asn Pro His Phe Leu Asp Gly Arg Asp  
 145 150 155 160  
 Ile Asn Gly Arg Met Arg Ala Ile Leu Val Asp Trp Leu Val Gln Val  
 165 170 175  
 His Ser Lys Phe Arg Leu Leu Gln Glu Thr Leu Tyr Met Cys Val Gly  
 180 185 190  
 Ile Met Asp Arg Phe Leu Gln Val Gln Pro Val Ser Arg Lys Lys Leu  
 195 200 205  
 Gln Leu Val Gly Ile Thr Ala Leu Leu Leu Ala Ser Lys Tyr Glu Glu  
 210 215 220  
 Met Phe Ser Pro Asn Ile Glu Asp Phe Val Tyr Ile Thr Asp Asn Ala  
 225 230 235 240  
 Tyr Thr Ser Ser Gln Ile Arg Glu Met Glu Thr Leu Ile Leu Lys Glu  
 245 250 255  
 Leu Lys Phe Glu Leu Gly Arg Pro Leu Pro Leu His Phe Leu Arg Arg  
 260 265 270  
 Ala Ser Lys Ala Gly Glu Val Asp Val Glu Gln His Thr Leu Ala Lys  
 275 280 285  
 Tyr Leu Met Glu Leu Thr Leu Ile Asp Tyr Asp Met Val His Tyr His  
 290 295 300  
 Pro Ser Lys Val Ala Ala Ala Ser Cys Leu Ser Gln Lys Val Leu  
 305 310 315 320  
 Gly Gln Gly Lys Trp Asn Leu Lys Gln Gln Tyr Tyr Thr Gly Tyr Thr  
 325 330 335  
 Glu Asn Glu Val Leu Glu Val Met Gln His Met Ala Lys Asn Val Val  
 340 345 350  
 Lys Val Asn Glu Asn Leu Thr Lys Phe Ile Ala Ile Lys Asn Lys Tyr  
 355 360 365  
 Ala Ser Ser Lys Leu Leu Lys Ile Ser Met Ile Pro Gln Leu Asn Ser  
 370 375 380  
 Lys Ala Val Lys Asp Leu Ala Ser Pro Leu Ile Gly Arg Ser  
 385 390 395

<210> 188

<211> 376

<212> PRT

<213> Homo sapiens

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&lt;400&gt; 188

Met Gln Trp Ala Ser Leu Leu Leu Leu Ala Gly Leu Phe Ser Leu Ser  
 1 5 10 15  
 Gln Ala Gln Tyr Glu Asp Asp Pro His Trp Trp Phe His Tyr Leu Arg  
 20 25 30  
 Ser Gln Gln Ser Thr Tyr Tyr Asp Pro Tyr Asp Pro Tyr Pro Tyr Glu  
 35 40 45  
 Thr Tyr Glu Pro Tyr Pro Tyr Gly Val Asp Glu Gly Pro Ala Tyr Thr  
 50 55 60  
 Tyr Gly Ser Pro Ser Pro Pro Asp Pro Arg Asp Cys Pro Gln Glu Cys  
 65 70 75 80  
 Asp Cys Pro Pro Asn Phe Leu Thr Ala Met Tyr Cys Asp Asn Arg Asn  
 85 90 95  
 Leu Lys Tyr Leu Pro Phe Val Pro Ser Arg Met Lys Tyr Val Tyr Phe  
 100 105 110  
 Gln Asn Asn Gln Ile Thr Ser Ile Gln Glu Gly Val Phe Asp Asn Ala  
 115 120 125  
 Thr Gly Leu Leu Trp Ile Ala Leu His Gly Asn Gln Ile Thr Ser Asp  
 130 135 140  
 Lys Val Gly Arg Lys Val Phe Ser Lys Leu Arg His Leu Glu Arg Leu  
 145 150 155 160  
 Tyr Leu Asp His Asn Asn Leu Thr Arg Met Pro Gly Pro Leu Pro Arg  
 165 170 175  
 Ser Leu Arg Glu Leu His Leu Asp His Asn Gln Ile Ser Arg Val Pro  
 180 185 190  
 Asn Asn Ala Leu Glu Gly Leu Glu Asn Leu Thr Ala Leu Tyr Leu Gln  
 195 200 205  
 His Asp Glu Ile Gln Glu Val Gly Ser Ser Met Arg Gly Leu Arg Ser  
 210 215 220  
 Leu Ile Leu Leu Asp Leu Ser Tyr Asn His Leu Arg Lys Val Pro Asp  
 225 230 235 240  
 Gly Leu Pro Ser Ala Leu Glu Gln Leu Tyr Met Glu His Asn Asn Val  
 245 250 255  
 Tyr Thr Val Pro Asp Ser Tyr Phe Arg Gly Ala Pro Lys Leu Leu Tyr  
 260 265 270  
 Val Arg Leu Ser His Asn Ser Leu Thr Asn Asn Gly Leu Ala Ser Asn  
 275 280 285  
 Thr Phe Asn Ser Ser Ser Leu Leu Glu Leu Asp Leu Ser Tyr Asn Gln  
 290 295 300  
 Leu Gln Lys Ile Pro Pro Val Asn Thr Asn Leu Glu Asn Leu Tyr Leu  
 305 310 315 320  
 Gln Gly Asn Arg Ile Asn Glu Phe Ser Ile Ser Ser Phe Cys Thr Val  
 325 330 335  
 Val Asp Val Val Asn Phe Ser Lys Leu Gln Val Val Arg Leu Asp Gly  
 340 345 350  
 Asn Glu Ile Lys Arg Ser Ala Met Pro Ala Asp Ala Pro Leu Cys Leu  
 355 360 365  
 Arg Leu Ala Ser Leu Ile Glu Ile  
 370 375

&lt;210&gt; 189

&lt;211&gt; 535

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 189

Met Glu Glu Gly Ala Arg His Arg Asn Asn Thr Glu Lys Lys His Pro  
 1 5 10 15

Gly Gly Gly Glu Ser Asp Ala Ser Pro Glu Ala Gly Ser Gly Gly Gly  
 20 25 30  
 Gly Val Ala Leu Lys Lys Glu Ile Gly Leu Val Ser Ala Cys Gly Ile  
 35 40 45  
 Ile Val Gly Asn Ile Ile Gly Ser Gly Ile Phe Val Ser Pro Lys Gly  
 50 55 60  
 Val Leu Glu Asn Ala Gly Ser Val Gly Leu Ala Leu Ile Val Trp Ile  
 65 70 75 80  
 Val Thr Gly Phe Ile Thr Val Val Gly Ala Leu Cys Tyr Ala Glu Leu  
 85 90 95  
 Gly Val Thr Ile Pro Lys Ser Gly Gly Asp Tyr Ser Tyr Val Lys Asp  
 100 105 110  
 Ile Phe Gly Gly Leu Ala Gly Phe Leu Arg Leu Trp Ile Ala Val Leu  
 115 120 125  
 Val Ile Tyr Pro Thr Asn Gln Ala Val Ile Ala Leu Thr Phe Ser Asn  
 130 135 140  
 Tyr Val Leu Gln Pro Leu Phe Pro Thr Cys Phe Pro Glu Ser Gly  
 145 150 155 160  
 Leu Arg Leu Leu Ala Ala Ile Cys Leu Leu Leu Leu Thr Trp Val Asn  
 165 170 175  
 Cys Ser Ser Val Arg Trp Ala Thr Arg Val Gln Asp Ile Phe Thr Ala  
 180 185 190  
 Gly Lys Leu Leu Ala Leu Ala Leu Ile Ile Ile Met Gly Ile Val Gln  
 195 200 205  
 Ile Cys Lys Gly Glu Tyr Phe Trp Leu Glu Pro Lys Asn Ala Phe Glu  
 210 215 220  
 Asn Phe Gln Glu Pro Asp Ile Gly Leu Val Ala Leu Ala Phe Leu Gln  
 225 230 235 240  
 Gly Ser Phe Ala Tyr Gly Gly Trp Asn Phe Leu Asn Tyr Val Thr Glu  
 245 250 255  
 Glu Leu Val Asp Pro Tyr Lys Asn Leu Pro Arg Ala Ile Phe Ile Ser  
 260 265 270  
 Ile Pro Leu Val Thr Phe Val Tyr Val Phe Ala Asn Val Ala Tyr Val  
 275 280 285  
 Thr Ala Met Ser Pro Gln Glu Leu Leu Ala Ser Asn Ala Val Ala Val  
 290 295 300  
 Thr Phe Gly Glu Lys Leu Leu Gly Val Met Ala Trp Ile Met Pro Ile  
 305 310 315 320  
 Ser Val Ala Leu Ser Thr Phe Gly Gly Val Asn Gly Ser Leu Phe Thr  
 325 330 335  
 Ser Ser Arg Leu Phe Phe Ala Gly Ala Arg Glu Gly His Leu Pro Ser  
 340 345 350  
 Val Leu Ala Met Ile His Val Lys Arg Cys Thr Pro Ile Pro Ala Leu  
 355 360 365  
 Leu Phe Thr Cys Ile Ser Thr Leu Leu Met Leu Val Thr Ser Asp Met  
 370 375 380  
 Tyr Thr Leu Ile Asn Tyr Val Gly Phe Ile Asn Tyr Leu Phe Tyr Gly  
 385 390 395 400  
 Val Thr Val Ala Gly Gln Ile Val Leu Arg Trp Lys Lys Pro Asp Ile  
 405 410 415  
 Pro Arg Pro Ile Lys Ile Asn Leu Leu Phe Pro Ile Ile Tyr Leu Leu  
 420 425 430  
 Phe Trp Ala Phe Leu Leu Val Phe Ser Leu Trp Ser Glu Pro Val Val  
 435 440 445  
 Cys Gly Ile Gly Leu Ala Ile Met Leu Thr Gly Val Pro Val Tyr Phe  
 450 455 460  
 Leu Gly Val Tyr Trp Gln His Lys Pro Lys Cys Phe Ser Asp Phe Ile  
 465 470 475 480  
 Glu Leu Leu Thr Leu Val Ser Gln Lys Met Cys Val Val Val Tyr Pro  
 485 490 495  
 Glu Val Glu Arg Gly Ser Gly Thr Glu Ala Asn Glu Asp Met Glu  
 500 505 510

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Glu Gln Gln Gln Pro Met Tyr Gln Pro Thr Pro Thr Lys Asp Lys Asp  
 515 520 525  
 Val Ala Gly Gln Pro Gln Pro  
 530 535

&lt;210&gt; 190

&lt;211&gt; 225

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 190

Met Asn Ser Asn Val Glu Asn Leu Pro Pro His Ile Ile Arg Leu Val  
 1 5 10 15  
 Tyr Lys Glu Val Thr Thr Leu Thr Ala Asp Pro Pro Asp Gly Ile Lys  
 20 25 30  
 Val Phe Pro Asn Glu Glu Asp Leu Thr Asp Leu Gln Val Thr Ile Glu  
 35 40 45  
 Gly Pro Glu Gly Thr Pro Tyr Ala Gly Gly Leu Phe Arg Met Lys Leu  
 50 55 60  
 Leu Leu Gly Lys Asp Phe Pro Ala Ser Pro Pro Lys Gly Tyr Phe Leu  
 65 70 75 80  
 Thr Lys Ile Phe His Pro Asn Val Gly Ala Asn Gly Glu Ile Cys Val  
 85 90 95  
 Asn Val Leu Lys Arg Asp Trp Thr Ala Glu Leu Gly Ile Arg His Val  
 100 105 110  
 Leu Leu Thr Ile Lys Cys Leu Leu Ile His Pro Asn Pro Glu Ser Ala  
 115 120 125  
 Leu Asn Glu Glu Ala Gly Arg Leu Leu Leu Glu Asn Tyr Glu Glu Tyr  
 130 135 140  
 Ala Ala Arg Ala Arg Leu Leu Thr Glu Ile His Gly Ala Gly Gly  
 145 150 155 160  
 Pro Ser Gly Arg Ala Glu Ala Gly Arg Ala Leu Ala Ser Gly Thr Glu  
 165 170 175  
 Ala Ser Ser Thr Asp Pro Gly Ala Pro Gly Gly Pro Gly Gly Ala Glu  
 180 185 190  
 Gly Pro Met Ala Lys Lys His Ala Gly Glu Arg Asp Lys Lys Leu Ala  
 195 200 205  
 Ala Lys Lys Lys Thr Asp Lys Lys Arg Ala Leu Arg Ala Leu Arg Arg  
 210 215 220  
 Leu  
 225

&lt;210&gt; 191

&lt;211&gt; 485

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 191

Met Arg Lys Arg Ala Pro Gln Ser Glu Met Ala Pro Ala Gly Val Ser  
 1 5 10 15  
 Leu Arg Ala Thr Ile Leu Cys Leu Leu Ala Trp Ala Gly Leu Ala Ala  
 20 25 30  
 Gly Asp Arg Val Tyr Ile His Pro Phe His Leu Val Ile His Asn Glu  
 35 40 45

Ser	Thr	Cys	Glu	Gln	Leu	Ala	Lys	Ala	Asn	Ala	Gly	Lys	Pro	Lys	Asp
50						55				60					
Pro	Thr	Phe	Ile	Pro	Ala	Pro	Ile	Gln	Ala	Lys	Thr	Ser	Pro	Val	Asp
65					70					75					80
Glu	Lys	Ala	Leu	Gln	Asp	Gln	Leu	Val	Leu	Val	Ala	Ala	Lys	Leu	Asp
				85					90					95	
Thr	Glu	Asp	Lys	Leu	Arg	Ala	Ala	Met	Val	Gly	Met	Leu	Ala	Asn	Phe
			100					105					110		
Leu	Gly	Phe	Arg	Ile	Tyr	Gly	Met	His	Ser	Glu	Leu	Trp	Gly	Val	Val
		115				120						125			
His	Gly	Ala	Thr	Val	Leu	Ser	Pro	Thr	Ala	Val	Phe	Gly	Thr	Leu	Ala
						135					140				
Ser	Leu	Tyr	Leu	Gly	Ala	Leu	Asp	His	Thr	Ala	Asp	Arg	Leu	Gln	Ala
145					150					155					160
Ile	Leu	Gly	Val	Pro	Trp	Lys	Asp	Lys	Asn	Cys	Thr	Ser	Arg	Leu	Asp
				165					170					175	
Ala	His	Lys	Val	Leu	Ser	Ala	Leu	Gln	Ala	Val	Gln	Gly	Leu	Leu	Val
			180					185					190		
Ala	Gln	Gly	Arg	Ala	Asp	Ser	Gln	Ala	Gln	Leu	Leu	Leu	Ser	Thr	Val
		195					200					205			
Val	Gly	Val	Phe	Thr	Ala	Pro	Gly	Leu	His	Leu	Lys	Gln	Pro	Phe	Val
						215					220				
Gln	Gly	Leu	Ala	Leu	Tyr	Thr	Pro	Val	Val	Leu	Pro	Arg	Ser	Leu	Asp
225					230					235					240
Phe	Thr	Glu	Leu	Asp	Val	Ala	Ala	Glu	Lys	Ile	Asp	Arg	Phe	Met	Gln
				245					250					255	
Ala	Val	Thr	Gly	Trp	Lys	Thr	Gly	Cys	Ser	Leu	Met	Gly	Ala	Ser	Val
			260					265					270		
Asp	Ser	Thr	Leu	Ala	Phe	Asn	Thr	Tyr	Val	His	Phe	Gln	Gly	Lys	Met
		275					280					285			
Lys	Gly	Phe	Ser	Leu	Leu	Ala	Glu	Pro	Gln	Glu	Phe	Trp	Val	Asp	Asn
						295					300				
Ser	Thr	Ser	Val	Ser	Val	Pro	Met	Leu	Ser	Gly	Met	Gly	Thr	Phe	Gln
305					310					315					320
His	Trp	Ser	Asp	Ile	Gln	Asp	Asn	Phe	Ser	Val	Thr	Gln	Val	Pro	Phe
				325					330					335	
Thr	Glu	Ser	Ala	Cys	Leu	Leu	Leu	Ile	Gln	Pro	His	Tyr	Ala	Ser	Asp
			340					345					350		
Leu	Asp	Lys	Val	Glu	Gly	Leu	Thr	Phe	Gln	Gln	Asn	Ser	Leu	Asn	Trp
		355					360					365			
Met	Lys	Lys	Leu	Ser	Pro	Arg	Thr	Ile	His	Leu	Thr	Met	Pro	Gln	Leu
					375						380				
Val	Leu	Gln	Gly	Ser	Tyr	Asp	Leu	Gln	Asp	Leu	Leu	Ala	Gln	Ala	Glu
385					390					395					400
Leu	Pro	Ala													

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&lt;210&gt; 192

&lt;211&gt; 279

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 192

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Met Thr Glu Arg Phe Asp Cys His His Cys Asn Glu Ser Leu Phe Gly
1      5      10      15
Lys Lys Tyr Ile Leu Arg Glu Glu Ser Pro Tyr Cys Val Val Cys Phe
20      25      30
Glu Thr Leu Phe Ala Asn Thr Cys Glu Glu Cys Gly Lys Pro Ile Gly
35      40      45
Cys Asp Cys Lys Asp Leu Ser Tyr Lys Asp Arg His Trp His Glu Ala
50      55      60
Cys Phe His Cys Ser Gln Cys Arg Asn Ser Leu Val Asp Lys Pro Phe
65      70      75      80
Ala Ala Lys Glu Asp Gln Leu Leu Cys Thr Asp Cys Tyr Ser Asn Glu
85      90      95
Tyr Ser Ser Lys Cys Gln Glu Cys Lys Lys Thr Ile Met Pro Gly Thr
100      105      110
Arg Lys Met Glu Tyr Lys Gly Ser Ser Trp His Glu Thr Cys Phe Ile
115      120      125
Cys His Arg Cys Gln Gln Pro Ile Gly Thr Lys Ser Phe Ile Pro Lys
130      135      140
Asp Asn Gln Asn Phe Cys Val Pro Cys Tyr Glu Lys Gln His Ala Met
145      150      155      160
Gln Cys Val Gln Cys Lys Lys Pro Ile Thr Thr Gly Gly Val Thr Tyr
165      170      175
Arg Glu Gln Pro Trp His Lys Glu Cys Phe Val Cys Thr Ala Cys Arg
180      185      190
Lys Gln Leu Ser Gly Gln Arg Phe Thr Ala Arg Asp Asp Phe Ala Tyr
195      200      205
Cys Leu Asn Cys Phe Cys Asp Leu Tyr Ala Lys Lys Cys Ala Gly Cys
210      215      220
Thr Asn Pro Ile Ser Gly Leu Gly Gly Thr Lys Tyr Ile Ser Phe Glu
225      230      235      240
Glu Arg Gln Trp His Asn Asp Cys Phe Asn Cys Lys Lys Cys Ser Leu
245      250      255
Ser Leu Val Gly Arg Gly Phe Leu Thr Glu Arg Asp Asp Ile Leu Cys
260      265      270
Pro Asp Cys Gly Lys Asp Ile
275

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&lt;210&gt; 193

&lt;211&gt; 738

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 193

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Met Glu Lys Ser Arg Met Asn Leu Pro Lys Gly Pro Asp Thr Leu Cys
1      5      10      15
Phe Asp Lys Asp Glu Phe Met Lys Glu Asp Phe Asp Val Asp His Phe
20      25      30

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Val Ser Asp Cys Arg Lys Arg Val Gln Leu Glu Glu Leu Arg Asp Asp  
 35 40 45  
 Leu Glu Leu Tyr Tyr Lys Leu Leu Lys Thr Ala Met Val Glu Leu Ile  
 50 55 60  
 Asn Lys Asp Tyr Ala Asp Phe Val Asn Leu Ser Thr Asn Leu Val Gly  
 65 70 75 80  
 Met Asp Lys Ala Leu Asn Gln Leu Ser Val Pro Leu Gly Gln Leu Arg  
 85 90 95  
 Glu Glu Val Leu Ser Leu Arg Ser Ser Val Ser Glu Gly Ile Arg Ala  
 100 105 110  
 Val Asp Glu Arg Met Ser Lys Gln Glu Asp Ile Arg Lys Lys Met  
 115 120 125  
 Cys Val Leu Arg Leu Ile Gln Val Ile Arg Ser Val Glu Lys Ile Glu  
 130 135 140  
 Lys Ile Leu Asn Ser Gln Ser Ser Lys Glu Thr Ser Ala Leu Glu Ala  
 145 150 155 160  
 Ser Ser Pro Leu Leu Thr Gly Gln Ile Leu Glu Arg Ile Ala Thr Glu  
 165 170 175  
 Phe Asn Gln Leu Gln Phe His Ala Val Gln Ser Lys Gly Met Pro Leu  
 180 185 190  
 Leu Asp Lys Val Arg Pro Arg Ile Ala Gly Ile Thr Ala Met Leu Gln  
 195 200 205  
 Gln Ser Leu Glu Gly Leu Leu Leu Glu Gly Leu Gln Thr Ser Asp Val  
 210 215 220  
 Asp Ile Ile Arg His Cys Leu Arg Thr Tyr Ala Thr Ile Asp Lys Thr  
 225 230 235 240  
 Arg Asp Ala Glu Ala Leu Val Gly Gln Val Leu Val Lys Pro Tyr Ile  
 245 250 255  
 Asp Glu Val Ile Ile Glu Gln Phe Val Glu Ser His Pro Asn Gly Leu  
 260 265 270  
 Gln Val Met Tyr Asn Lys Leu Leu Glu Phe Val Pro His His Cys Arg  
 275 280 285  
 Leu Leu Arg Glu Val Thr Gly Glu Ala Ile Ser Ser Glu Lys Gly Asn  
 290 295 300  
 Thr Val Pro Gly Tyr Asp Phe Leu Val Asn Ser Val Trp Pro Gln Ile  
 305 310 315 320  
 Val Gln Gly Leu Glu Lys Leu Pro Ser Leu Phe Asn Pro Gly Asn  
 325 330 335  
 Pro Asp Ala Phe His Glu Lys Tyr Thr Ile Ser Met Asp Phe Val Arg  
 340 345 350  
 Arg Leu Glu Arg Gln Cys Gly Ser Gln Ala Ser Val Lys Arg Leu Arg  
 355 360 365  
 Ala His Pro Ala Tyr His Ser Phe Asn Lys Lys Trp Asn Leu Pro Val  
 370 375 380  
 Tyr Phe Gln Ile Arg Phe Arg Glu Ile Ala Gly Ser Leu Glu Ala Ala  
 385 390 395 400  
 Leu Thr Asp Val Leu Glu Asp Ala Pro Ala Glu Ser Pro Tyr Cys Leu  
 405 410 415  
 Leu Ala Ser His Arg Thr Trp Ser Ser Leu Arg Arg Cys Trp Ser Asp  
 420 425 430  
 Glu Met Phe Leu Pro Leu Leu Val His Arg Leu Trp Arg Leu Thr Leu  
 435 440 445  
 Gln Ile Leu Ala Arg Tyr Ser Val Phe Val Asn Glu Leu Ser Leu Arg  
 450 455 460  
 Pro Ile Ser Asn Glu Ser Pro Lys Glu Ile Lys Lys Pro Leu Val Thr  
 465 470 475 480  
 Gly Ser Lys Glu Pro Ser Ile Thr Gln Gly Asn Thr Glu Asp Gln Gly  
 485 490 495  
 Ser Gly Pro Ser Glu Thr Lys Pro Val Val Ser Ile Ser Arg Thr Gln  
 500 505 510  
 Leu Val Tyr Val Val Ala Asp Leu Asp Lys Leu Gln Glu Gln Leu Pro  
 515 520 525

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Glu Leu Leu Glu Ile Ile Lys Pro Lys Leu Glu Met Ile Gly Phe Lys  
 530 535 540  
 Asn Phe Ser Ser Ile Ser Ala Ala Leu Glu Asp Ser Gln Ser Ser Phe  
 545 550 555 560  
 Ser Ala Cys Val Pro Ser Leu Ser Ser Lys Ile Ile Gln Asp Leu Ser  
 565 570 575  
 Asp Ser Cys Phe Gly Phe Leu Lys Ser Ala Leu Glu Val Pro Arg Leu  
 580 585 590  
 Tyr Arg Arg Thr Asn Lys Glu Val Pro Thr Thr Ala Ser Ser Tyr Val  
 595 600 605  
 Asp Ser Ala Leu Lys Pro Leu Phe Gln Leu Gln Ser Gly His Lys Asp  
 610 615 620  
 Lys Leu Lys Gln Ala Ile Ile Gln Gln Trp Leu Glu Gly Thr Leu Ser  
 625 630 635 640  
 Glu Ser Thr His Lys Tyr Tyr Glu Thr Val Ser Asp Val Leu Asn Ser  
 645 650 655  
 Val Lys Lys Met Glu Glu Ser Leu Lys Arg Leu Lys Gln Ala Arg Lys  
 660 665 670  
 Thr Thr Pro Ala Asn Pro Val Gly Pro Ser Gly Gly Met Ser Asp Asp  
 675 680 685  
 Asp Lys Ile Arg Leu Gln Leu Ala Leu Asp Val Glu Tyr Leu Gly Glu  
 690 695 700  
 Gln Ile Gln Lys Leu Gly Leu Gln Ala Ser Asp Ile Lys Ser Phe Ser  
 705 710 715 720  
 Ala Leu Ala Glu Leu Val Ala Ala Ala Lys Asp Gln Ala Thr Ala Glu  
 725 730 735  
 Gln Pro

&lt;210&gt; 194

&lt;211&gt; 963

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 194  
 Met Ala Val Phe Pro Trp His Ser Arg Asn Arg Asn Tyr Lys Ala Glu  
 1 5 10 15  
 Phe Ala Ser Cys Arg Leu Glu Ala Val Pro Leu Glu Phe Gly Asp Tyr  
 20 25 30  
 His Pro Leu Lys Pro Ile Thr Val Thr Glu Ser Lys Thr Lys Lys Val  
 35 40 45  
 Asn Arg Lys Gly Ser Thr Ser Ser Thr Ser Ser Ser Ser Ser Ser  
 50 55 60  
 Val Val Asp Pro Leu Ser Ser Val Leu Asp Gly Thr Asp Pro Leu Ser  
 65 70 75 80  
 Met Phe Ala Ala Thr Ala Asp Pro Ala Ala Leu Ala Ala Met Asp  
 85 90 95  
 Ser Ser Arg Arg Lys Arg Asp Arg Asp Asp Asn Ser Val Val Gly Ser  
 100 105 110  
 Asp Phe Glu Pro Trp Thr Asn Lys Arg Gly Glu Ile Leu Ala Arg Tyr  
 115 120 125  
 Thr Thr Thr Glu Lys Leu Ser Ile Asn Leu Phe Met Gly Ser Glu Lys  
 130 135 140  
 Gly Lys Ala Gly Thr Ala Thr Leu Ala Met Ser Glu Lys Val Arg Thr  
 145 150 155 160  
 Arg Leu Glu Glu Leu Asp Asp Phe Glu Glu Gly Ser Gln Lys Glu Leu  
 165 170 175

Leu Asn Leu Thr Gln Gln Asp Tyr Val Asn Arg Ile Glu Glu Leu Asn  
 180 185 190  
 Gln Ser Leu Lys Asp Ala Trp Ala Ser Asp Gln Lys Val Lys Ala Leu  
 195 200 205  
 Lys Ile Val Ile Gln Cys Ser Lys Leu Leu Ser Asp Thr Ser Val Ile  
 210 215 220  
 Gln Phe Tyr Pro Ser Lys Phe Val Leu Ile Thr Asp Ile Leu Asp Thr  
 225 230 235 240  
 Phe Gly Lys Leu Val Tyr Glu Arg Ile Phe Ser Met Cys Val Asp Ser  
 245 250 255  
 Arg Ser Val Leu Pro Asp His Phe Ser Pro Glu Asn Ala Asn Asp Thr  
 260 265 270  
 Ala Lys Glu Thr Cys Leu Asn Trp Phe Phe Lys Ile Ala Ser Ile Arg  
 275 280 285  
 Glu Leu Ile Pro Arg Phe Tyr Val Glu Ala Ser Ile Leu Lys Cys Asn  
 290 295 300  
 Lys Phe Leu Ser Lys Thr Gly Ile Ser Glu Cys Leu Pro Arg Leu Thr  
 305 310 315 320  
 Cys Met Ile Arg Gly Ile Gly Asp Pro Leu Val Ser Val Tyr Ala Arg  
 325 330 335  
 Ala Tyr Leu Cys Arg Val Gly Met Glu Val Ala Pro His Leu Lys Glu  
 340 345 350  
 Thr Leu Asn Lys Asn Phe Phe Asp Phe Leu Leu Thr Phe Lys Gln Ile  
 355 360 365  
 His Gly Asp Thr Val Gln Asn Gln Leu Val Val Gln Gly Val Glu Leu  
 370 375 380  
 Pro Ser Tyr Leu Pro Leu Tyr Pro Pro Ala Met Asp Trp Ile Phe Gln  
 385 390 395 400  
 Cys Ile Ser Tyr His Ala Pro Glu Ala Leu Leu Thr Glu Met Met Glu  
 405 410 415  
 Arg Cys Lys Lys Leu Gly Asn Asn Ala Leu Leu Leu Asn Ser Val Met  
 420 425 430  
 Ser Ala Phe Arg Ala Glu Phe Ile Ala Thr Arg Ser Met Asp Phe Ile  
 435 440 445  
 Gly Met Ile Lys Glu Cys Asp Glu Ser Gly Phe Pro Lys His Leu Leu  
 450 455 460  
 Phe Arg Ser Leu Gly Leu Asn Leu Ala Leu Ala Asp Pro Pro Glu Ser  
 465 470 475 480  
 Asp Arg Leu Gln Ile Leu Asn Glu Ala Trp Lys Val Ile Thr Lys Leu  
 485 490 495  
 Lys Asn Pro Gln Asp Tyr Ile Asn Cys Ala Glu Val Trp Val Glu Tyr  
 500 505 510  
 Thr Cys Lys His Phe Thr Lys Arg Glu Val Asn Thr Val Leu Ala Asp  
 515 520 525  
 Val Ile Lys His Met Thr Pro Asp Arg Ala Phe Glu Asp Ser Tyr Pro  
 530 535 540  
 Gln Leu Gln Leu Ile Ile Lys Lys Val Ile Ala His Phe His Asp Phe  
 545 550 555 560  
 Ser Val Leu Phe Ser Val Glu Lys Phe Leu Pro Phe Leu Asp Met Phe  
 565 570 575  
 Gln Lys Glu Ser Val Arg Val Glu Val Cys Lys Cys Ile Met Asp Ala  
 580 585 590  
 Phe Ile Lys His Gln Gln Glu Pro Thr Lys Asp Pro Val Ile Leu Asn  
 595 600 605  
 Ala Leu Leu His Val Cys Lys Thr Met His Asp Ser Val Asn Ala Leu  
 610 615 620  
 Thr Leu Glu Asp Glu Lys Arg Met Leu Ser Tyr Leu Ile Asn Gly Phe  
 625 630 635 640  
 Ile Lys Met Val Ser Phe Gly Arg Asp Phe Glu Gln Gln Leu Ser Phe  
 645 650 655  
 Tyr Val Glu Ser Arg Ser Met Phe Cys Asn Leu Glu Pro Val Leu Val  
 660 665 670

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Gln Leu Ile His Ser Val Asn Arg Leu Ala Met Glu Thr Arg Lys Val  
 675 680 685  
 Met Lys Gly Asn His Ser Arg Lys Thr Ala Ala Phe Val Arg Ala Cys  
 690 695 700  
 Val Ala Tyr Cys Phe Ile Thr Ile Pro Ser Leu Ala Gly Ile Phe Thr  
 705 710 715 720  
 Arg Leu Asn Leu Tyr Leu His Ser Gly Gln Val Ala Leu Ala Asn Gln  
 725 730 735  
 Cys Leu Ser Gln Ala Asp Ala Phe Phe Lys Ala Ala Ile Ser Leu Val  
 740 745 750  
 Pro Glu Val Pro Lys Met Ile Asn Ile Asp Gly Lys Met Arg Pro Ser  
 755 760 765  
 Glu Ser Phe Leu Leu Glu Phe Leu Cys Asn Phe Phe Ser Thr Leu Leu  
 770 775 780  
 Ile Val Pro Asp His Pro Glu His Gly Val Leu Phe Leu Val Arg Glu  
 785 790 795 800  
 Leu Leu Asn Val Ile Gln Asp Tyr Thr Trp Glu Asp Asn Ser Asp Glu  
 805 810 815  
 Lys Ile Arg Ile Tyr Thr Cys Val Leu His Leu Leu Ser Ala Met Ser  
 820 825 830  
 Gln Glu Thr Tyr Leu Tyr His Ile Asp Lys Val Asp Ser Asn Asp Ser  
 835 840 845  
 Leu Tyr Gly Gly Asp Ser Lys Phe Leu Ala Glu Asn Asn Lys Leu Cys  
 850 855 860  
 Glu Thr Val Met Ala Gln Ile Leu Glu His Leu Lys Thr Leu Ala Lys  
 865 870 875 880  
 Asp Glu Ala Leu Lys Arg Gln Ser Ser Leu Gly Leu Ser Phe Phe Asn  
 885 890 895  
 Ser Ile Leu Ala His Gly Asp Leu Arg Asn Asn Lys Leu Asn Gln Leu  
 900 905 910  
 Ser Val Asn Leu Trp His Leu Ala Gln Arg His Gly Cys Ala Asp Thr  
 915 920 925  
 Arg Thr Met Val Lys Thr Leu Glu Tyr Ile Lys Lys Gln Ser Lys Gln  
 930 935 940  
 Pro Asp Met Thr His Leu Thr Glu Leu Ala Leu Arg Leu Pro Leu Gln  
 945 950 955 960  
 Thr Arg Thr

&lt;210&gt; 195

&lt;211&gt; 494

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 195

Met Phe Glu Ile Lys Lys Ile Cys Cys Ile Gly Ala Gly Tyr Val Gly  
 1 5 10 15  
 Gly Pro Thr Cys Ser Val Ile Ala His Met Cys Pro Glu Ile Arg Val  
 20 25 30  
 Thr Val Val Asp Val Asn Glu Ser Arg Ile Asn Ala Trp Asn Ser Pro  
 35 40 45  
 Thr Leu Pro Ile Tyr Glu Pro Gly Leu Lys Glu Val Val Glu Ser Cys  
 50 55 60  
 Arg Gly Lys Asn Leu Phe Phe Ser Thr Asn Ile Asp Asp Ala Ile Lys  
 65 70 75 80  
 Glu Ala Asp Leu Val Phe Ile Ser Val Asn Thr Pro Thr Lys Thr Tyr  
 85 90 95

Gly Met Gly Lys Gly Arg Ala Ala Asp Leu Lys Tyr Ile Glu Ala Cys  
 100 105 110  
 Ala Arg Arg Ile Val Gln Asn Ser Asn Gly Tyr Lys Ile Val Thr Glu  
 115 120 125  
 Lys Ser Thr Val Pro Val Arg Ala Ala Glu Ser Ile Arg Arg Ile Phe  
 130 135 140  
 Asp Ala Asn Thr Lys Pro Asn Leu Asn Leu Gln Val Leu Ser Asn Pro  
 145 150 155 160  
 Glu Phe Leu Ala Glu Gly Thr Ala Ile Lys Asp Leu Lys Asn Pro Asp  
 165 170 175  
 Arg Val Leu Ile Gly Gly Asp Glu Thr Pro Glu Gly Gln Arg Ala Val  
 180 185 190  
 Gln Ala Leu Cys Ala Val Tyr Glu His Trp Val Pro Arg Glu Lys Ile  
 195 200 205  
 Leu Thr Thr Asn Thr Trp Ser Ser Glu Leu Ser Lys Leu Ala Ala Asn  
 210 215 220  
 Ala Phe Leu Ala Gln Arg Ile Ser Ser Ile Asn Ser Ile Ser Ala Leu  
 225 230 235 240  
 Cys Glu Ala Thr Gly Ala Asp Val Glu Glu Val Ala Thr Ala Ile Gly  
 245 250 255  
 Met Asp Gln Arg Ile Gly Asn Lys Phe Leu Lys Ala Ser Val Gly Phe  
 260 265 270  
 Gly Gly Ser Cys Phe Gln Lys Asp Val Leu Asn Leu Val Tyr Leu Cys  
 275 280 285  
 Glu Ala Leu Asn Leu Pro Glu Val Ala Arg Tyr Trp Gln Gln Val Ile  
 290 295 300  
 Asp Met Asn Asp Tyr Gln Arg Arg Arg Phe Ala Ser Arg Ile Ile Asp  
 305 310 315 320  
 Ser Leu Phe Asn Thr Val Thr Asp Lys Lys Ile Ala Ile Leu Gly Phe  
 325 330 335  
 Ala Phe Lys Lys Asp Thr Gly Asp Thr Arg Glu Ser Ser Ser Ile Tyr  
 340 345 350  
 Ile Ser Lys Tyr Leu Met Asp Glu Gly Ala His Leu His Ile Tyr Asp  
 355 360 365  
 Pro Lys Val Pro Arg Glu Gln Ile Val Val Asp Leu Ser His Pro Gly  
 370 375 380  
 Val Ser Glu Asp Asp Gln Val Ser Arg Leu Val Thr Ile Ser Lys Asp  
 385 390 395 400  
 Pro Tyr Glu Ala Cys Asp Gly Ala His Ala Val Val Ile Cys Thr Glu  
 405 410 415  
 Trp Asp Met Phe Lys Glu Leu Asp Tyr Glu Arg Ile His Lys Lys Met  
 420 425 430  
 Leu Lys Pro Ala Phe Ile Phe Asp Gly Arg Arg Val Leu Asp Gly Leu  
 435 440 445  
 His Asn Glu Leu Gln Thr Ile Gly Phe Gln Ile Glu Thr Ile Gly Lys  
 450 455 460  
 Lys Val Ser Ser Lys Arg Ile Pro Tyr Ala Pro Ser Gly Glu Ile Pro  
 465 470 475 480  
 Lys Phe Ser Leu Gln Asp Pro Pro Asn Lys Lys Pro Lys Val  
 485 490

&lt;210&gt; 196

&lt;211&gt; 205

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 196

Met Ala Leu Gln Leu Ser Arg Glu Gln Gly Ile Thr Leu Arg Gly Ser  
 1 5 10 15  
 Ala Glu Ile Val Ala Glu Phe Phe Ser Phe Gly Ile Asn Ser Ile Leu  
 20 25 30  
 Tyr Gln Arg Gly Ile Tyr Pro Ser Glu Thr Phe Thr Arg Val Gln Lys  
 35 40 45  
 Tyr Gly Leu Thr Leu Leu Val Thr Thr Asp Leu Glu Leu Ile Lys Tyr  
 50 55 60  
 Leu Asn Asn Val Val Glu Gln Leu Lys Asp Trp Leu Tyr Lys Cys Ser  
 65 70 75 80  
 Val Gln Lys Leu Val Val Val Ile Ser Asn Ile Glu Ser Gly Glu Val  
 85 90 95  
 Leu Glu Arg Trp Gln Phe Asp Ile Glu Cys Asp Lys Thr Ala Lys Asp  
 100 105 110  
 Asp Ser Ala Pro Arg Glu Lys Ser Gln Lys Ala Ile Gln Asp Glu Ile  
 115 120 125  
 Arg Ser Val Ile Arg Gln Ile Thr Ala Thr Val Thr Phe Leu Pro Leu  
 130 135 140  
 Leu Glu Val Ser Cys Ser Phe Asp Leu Leu Ile Tyr Thr Asp Lys Asp  
 145 150 155 160  
 Leu Val Val Pro Glu Lys Trp Glu Glu Ser Gly Pro Gln Phe Ile Thr  
 165 170 175  
 Asn Ser Glu Glu Val Arg Leu Arg Ser Phe Thr Thr Thr Ile His Lys  
 180 185 190  
 Val Asn Ser Met Val Ala Tyr Lys Ile Pro Val Asn Asp  
 195 200 205

&lt;210&gt; 197

&lt;211&gt; 427

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 197

Met Ala Pro Lys Lys Arg Pro Glu Thr Gln Lys Thr Ser Glu Ile Val  
 1 5 10 15  
 Leu Arg Pro Arg Asn Lys Arg Ser Arg Ser Pro Leu Glu Leu Glu Pro  
 20 25 30  
 Glu Ala Lys Lys Leu Cys Ala Lys Gly Ser Gly Pro Ser Arg Arg Cys  
 35 40 45  
 Asp Ser Asp Cys Leu Trp Val Gly Leu Ala Gly Pro Gln Ile Leu Pro  
 50 55 60  
 Pro Cys Arg Ser Ile Val Arg Thr Leu His Gln His Lys Leu Gly Arg  
 65 70 75 80  
 Ala Ser Trp Pro Ser Val Gln Gln Gly Leu Gln Gln Ser Phe Leu His  
 85 90 95  
 Thr Leu Asp Ser Tyr Arg Ile Leu Gln Lys Ala Ala Pro Phe Asp Arg  
 100 105 110  
 Arg Ala Thr Ser Leu Ala Trp His Pro Thr His Pro Ser Thr Val Ala  
 115 120 125  
 Val Gly Ser Lys Gly Gly Asp Ile Met Leu Trp Asn Phe Gly Ile Lys  
 130 135 140  
 Asp Lys Pro Thr Phe Ile Lys Gly Ile Gly Ala Gly Gly Ser Ile Thr  
 145 150 155 160  
 Gly Leu Lys Phe Asn Pro Leu Asn Thr Asn Gln Phe Tyr Ala Ser Ser  
 165 170 175

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Met Glu Gly Thr Thr Arg Leu Gln Asp Phe Lys Gly Asn Ile Leu Arg  
 180 185 190  
 Val Phe Ala Ser Ser Asp Thr Ile Asn Ile Trp Phe Cys Ser Leu Asp  
 195 200 205  
 Val Ser Ala Ser Ser Arg Met Val Val Thr Gly Asp Asn Val Gly Asn  
 210 215 220  
 Val Ile Leu Leu Asn Met Asp Gly Lys Glu Leu Trp Asn Leu Arg Met  
 225 230 235 240  
 His Lys Lys Lys Val Thr His Val Ala Leu Asn Pro Cys Cys Asp Trp  
 245 250 255  
 Phe Leu Ala Thr Ala Ser Val Asp Gln Thr Val Lys Ile Trp Asp Leu  
 260 265 270  
 Arg Gln Val Arg Gly Lys Ala Ser Phe Leu Tyr Ser Leu Pro His Arg  
 275 280 285  
 His Pro Val Asn Ala Ala Cys Phe Ser Pro Asp Gly Ala Arg Leu Leu  
 290 295 300  
 Thr Thr Asp Gln Lys Ser Glu Ile Arg Val Tyr Ser Ala Ser Gln Trp  
 305 310 315 320  
 Asp Cys Pro Leu Gly Leu Ile Pro His Pro His Arg His Phe Gln His  
 325 330 335  
 Leu Thr Pro Ile Lys Ala Ala Trp His Pro Arg Tyr Asn Leu Ile Val  
 340 345 350  
 Val Gly Arg Tyr Pro Asp Pro Asn Phe Lys Ser Cys Thr Pro Tyr Glu  
 355 360 365  
 Leu Arg Thr Ile Asp Val Phe Asp Gly Asn Ser Gly Lys Met Met Cys  
 370 375 380  
 Gln Leu Tyr Asp Pro Glu Ser Ser Gly Ile Ser Ser Leu Asn Glu Phe  
 385 390 395 400  
 Asn Pro Met Gly Asp Thr Leu Ala Ser Ala Met Gly Tyr His Ile Leu  
 405 410 415  
 Ile Trp Ser Gln Glu Glu Ala Arg Thr Arg Lys  
 420 425

&lt;210&gt; 198

&lt;211&gt; 283

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 198

Met Glu His Gly Ser Ile Ile Thr Gln Ala Arg Arg Glu Asp Ala Leu  
 1 5 10 15  
 Val Leu Thr Lys Gln Gly Leu Val Ser Lys Ser Ser Pro Lys Lys Pro  
 20 25 30  
 Arg Gly Arg Asn Ile Phe Lys Ala Leu Phe Cys Cys Phe Arg Ala Gln  
 35 40 45  
 His Val Gly Gln Ser Ser Ser Ser Thr Glu Leu Ala Tyr Lys Glu  
 50 55 60  
 Glu Ala Asn Thr Ile Ala Lys Ser Asp Leu Leu Gln Cys Leu Gln Tyr  
 65 70 75 80  
 Gln Phe Tyr Gln Ile Pro Gly Thr Cys Leu Leu Pro Glu Val Thr Glu  
 85 90 95  
 Glu Asp Gln Gly Arg Ile Cys Val Val Ile Asp Leu Asp Glu Thr Leu  
 100 105 110  
 Val His Ser Ser Phe Lys Pro Ile Asn Asn Ala Asp Phe Ile Val Pro  
 115 120 125  
 Ile Glu Ile Glu Gly Thr Thr His Gln Val Tyr Val Leu Lys Arg Pro  
 130 135 140

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Tyr Val Asp Glu Phe Leu Arg Arg Met Gly Glu Leu Phe Glu Cys Val  
 145 150 155 160  
 Leu Phe Thr Ala Ser Leu Ala Lys Tyr Ala Asp Pro Val Thr Asp Leu  
 165 170 175  
 Leu Asp Arg Cys Gly Val Phe Arg Ala Arg Leu Phe Arg Glu Ser Cys  
 180 185 190  
 Val Phe His Gln Gly Cys Tyr Val Lys Asp Leu Ser Arg Leu Gly Arg  
 195 200 205  
 Asp Leu Arg Lys Thr Leu Ile Leu Asp Asn Ser Pro Ala Ser Tyr Ile  
 210 215 220  
 Phe His Pro Glu Asn Ala Val Pro Val Gln Ser Trp Phe Asp Asp Met  
 225 230 235 240  
 Ala Asp Thr Glu Leu Leu Asn Leu Ile Pro Ile Phe Glu Glu Leu Ser  
 245 250 255  
 Gly Ala Glu Asp Val Tyr Thr Ser Leu Gly Ala Ala Ala Gly Pro Leu  
 260 265 270  
 Ala Cys Pro Ala Ser Lys Arg Arg Pro Ser Gln  
 275 280

&lt;210&gt; 199

&lt;211&gt; 239

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 199  
 Met Ala His Ala Gly Arg Thr Gly Tyr Asp Asn Arg Glu Ile Val Met  
 1 5 10 15  
 Lys Tyr Ile His Tyr Lys Leu Ser Gln Arg Gly Tyr Glu Trp Asp Ala  
 20 25 30  
 Gly Asp Val Gly Ala Ala Pro Pro Gly Ala Ala Pro Ala Pro Gly Ile  
 35 40 45  
 Phe Ser Ser Gln Pro Gly His Thr Pro His Thr Ala Ala Ser Arg Asp  
 50 55 60  
 Pro Val Ala Arg Thr Ser Pro Leu Gln Thr Pro Ala Ala Pro Gly Ala  
 65 70 75 80  
 Ala Ala Gly Pro Ala Leu Ser Pro Val Pro Pro Val Val His Leu Thr  
 85 90 95  
 Leu Arg Gln Ala Gly Asp Asp Phe Ser Arg Arg Tyr Arg Arg Asp Phe  
 100 105 110  
 Ala Glu Met Ser Arg Gln Leu His Leu Thr Pro Phe Thr Ala Arg Gly  
 115 120 125  
 Arg Phe Ala Thr Val Val Glu Glu Leu Phe Arg Asp Gly Val Asn Trp  
 130 135 140  
 Gly Arg Ile Val Ala Phe Phe Glu Phe Gly Gly Val Met Cys Val Glu  
 145 150 155 160  
 Ser Val Asn Arg Glu Met Ser Pro Leu Val Asp Asn Ile Ala Leu Trp  
 165 170 175  
 Met Thr Glu Tyr Leu Asn Arg His Leu His Thr Trp Ile Gln Asp Asn  
 180 185 190  
 Gly Gly Trp Asp Ala Phe Val Glu Leu Tyr Gly Pro Ser Met Arg Pro  
 195 200 205  
 Leu Phe Asp Phe Ser Trp Leu Ser Leu Lys Thr Leu Leu Ser Leu Ala  
 210 215 220  
 Leu Val Gly Ala Cys Ile Thr Leu Gly Ala Tyr Leu Gly His Lys  
 225 230 235



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&lt;210&gt; 200

&lt;211&gt; 751

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 200

Met Ala Phe Arg Thr Ile Cys Val Leu Val Gly Val Phe Ile Cys Ser  
 1 5 10 15  
 Ile Cys Val Lys Gly Ser Ser Gln Pro Gln Ala Arg Val Tyr Leu Thr  
 20 25 30  
 Phe Asp Glu Leu Arg Glu Thr Lys Thr Ser Glu Tyr Phe Ser Leu Ser  
 35 40 45  
 His His Pro Leu Asp Tyr Arg Ile Leu Leu Met Asp Glu Asp Gln Asp  
 50 55 60  
 Arg Ile Tyr Val Gly Ser Lys Asp His Ile Leu Ser Leu Asn Ile Asn  
 65 70 75 80  
 Asn Ile Ser Gln Glu Ala Leu Ser Val Phe Trp Pro Ala Ser Thr Ile  
 85 90 95  
 Lys Val Glu Glu Cys Lys Met Ala Gly Lys Asp Pro Thr His Gly Cys  
 100 105 110  
 Gly Asn Phe Val Arg Val Ile Gln Thr Phe Asn Arg Thr His Leu Tyr  
 115 120 125  
 Val Cys Gly Ser Gly Ala Phe Ser Pro Val Cys Thr Tyr Leu Asn Arg  
 130 135 140  
 Gly Arg Arg Ser Glu Asp Gln Val Phe Met Ile Asp Ser Lys Cys Glu  
 145 150 155 160  
 Ser Gly Lys Gly Arg Cys Ser Phe Asn Pro Asn Val Asn Thr Val Ser  
 165 170 175  
 Val Met Ile Asn Glu Glu Leu Phe Ser Gly Met Tyr Ile Asp Phe Met  
 180 185 190  
 Gly Thr Asp Ala Ala Ile Phe Arg Ser Leu Thr Lys Arg Asn Ala Val  
 195 200 205  
 Arg Thr Asp Gln His Asn Ser Lys Trp Leu Ser Glu Pro Met Phe Val  
 210 215 220  
 Asp Ala His Val Ile Pro Asp Gly Thr Asp Pro Asn Asp Ala Lys Val  
 225 230 235 240  
 Tyr Phe Phe Phe Lys Glu Lys Leu Thr Asp Asn Asn Arg Ser Thr Lys  
 245 250 255  
 Gln Ile His Ser Met Ile Ala Arg Ile Cys Pro Asn Asp Thr Gly Gly  
 260 265 270  
 Leu Arg Ser Leu Val Asn Lys Trp Thr Thr Phe Leu Lys Ala Arg Leu  
 275 280 285  
 Val Cys Ser Val Thr Asp Glu Asp Gly Pro Glu Thr His Phe Asp Glu  
 290 295 300  
 Leu Glu Asp Val Phe Leu Glu Thr Asp Asn Pro Arg Thr Thr Leu  
 305 310 315 320  
 Val Tyr Gly Ile Phe Thr Thr Ser Ser Ser Val Phe Lys Gly Ser Ala  
 325 330 335  
 Val Cys Val Tyr His Leu Ser Asp Ile Gln Thr Val Phe Asn Gly Pro  
 340 345 350  
 Phe Ala His Lys Glu Gly Pro Asn His Gln Leu Ile Ser Tyr Gln Gly  
 355 360 365  
 Arg Ile Pro Tyr Pro Arg Pro Gly Thr Cys Pro Gly Gly Ala Phe Thr  
 370 375 380  
 Pro Asn Met Arg Thr Thr Lys Glu Phe Pro Asp Asp Val Val Thr Phe  
 385 390 395 400

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Ile Arg Asn His Pro Leu Met Tyr Asn Ser Ile Tyr Pro Ile His Lys  
 405 410 415  
 Arg Pro Leu Ile Val Arg Ile Gly Thr Asp Tyr Lys Tyr Thr Lys Ile  
 420 425 430  
 Ala Val Asp Arg Val Asn Ala Ala Asp Gly Arg Tyr His Val Leu Phe  
 435 440 445  
 Leu Gly Thr Asp Arg Gly Thr Val Gln Lys Val Val Val Leu Pro Thr  
 450 455 460  
 Asn Asn Ser Val Ser Gly Glu Leu Ile Leu Glu Glu Leu Glu Val Phe  
 465 470 475 480  
 Lys Asn His Ala Pro Ile Thr Thr Met Lys Ile Ser Ser Lys Lys Gln  
 485 490 495  
 Gln Leu Tyr Val Ser Ser Asn Glu Gly Val Ser Gln Val Ser Leu His  
 500 505 510  
 Arg Cys His Ile Tyr Gly Thr Ala Cys Ala Asp Cys Cys Leu Ala Arg  
 515 520 525  
 Asp Pro Tyr Cys Ala Trp Asp Gly His Ser Cys Ser Arg Phe Tyr Pro  
 530 535 540  
 Thr Gly Lys Arg Arg Ser Arg Arg Gln Asp Val Arg His Gly Asn Pro  
 545 550 555 560  
 Leu Thr Gln Cys Arg Gly Phe Asn Leu Lys Ala Tyr Arg Asn Ala Ala  
 565 570 575  
 Glu Ile Val Gln Tyr Gly Val Lys Asn Asn Thr Thr Phe Leu Glu Cys  
 580 585 590  
 Ala Pro Lys Ser Pro Gln Ala Ser Ile Lys Trp Leu Leu Gln Lys Asp  
 595 600 605  
 Lys Asp Arg Arg Lys Glu Val Lys Leu Asn Glu Arg Ile Ile Ala Thr  
 610 615 620  
 Ser Gln Gly Leu Leu Ile Arg Ser Val Gln Gly Ser Asp Gln Gly Leu  
 625 630 635 640  
 Tyr His Cys Ile Ala Thr Glu Asn Ser Phe Lys Gln Thr Ile Ala Lys  
 645 650 655  
 Ile Asn Phe Lys Val Leu Asp Ser Glu Met Val Ala Val Val Thr Asp  
 660 665 670  
 Lys Trp Ser Pro Trp Thr Trp Ala Ser Ser Val Arg Ala Leu Pro Phe  
 675 680 685  
 His Pro Lys Asp Ile Met Gly Ala Phe Ser His Ser Glu Met Gln Met  
 690 695 700  
 Ile Asn Gln Tyr Cys Lys Asp Thr Arg Gln Gln His Gln Gln Gly Asp  
 705 710 715 720  
 Glu Ser Gln Lys Met Arg Gly Asp Tyr Gly Lys Leu Lys Ala Leu Ile  
 725 730 735  
 Asn Ser Arg Lys Ser Arg Asn Arg Arg Asn Gln Leu Pro Glu Ser  
 740 745 750

&lt;210&gt; 201

&lt;211&gt; 208

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 201

Met Lys Leu Leu Pro Ser Val Val Leu Lys Leu Phe Leu Ala Ala Val  
 1 5 10 15  
 Leu Ser Ala Leu Val Thr Gly Glu Ser Leu Glu Arg Leu Arg Arg Gly  
 20 25 30  
 Leu Ala Ala Gly Thr Ser Asn Pro Asp Pro Pro Thr Val Ser Thr Asp  
 35 40 45

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Gln Leu Leu Pro Leu Gly Gly Gly Arg Asp Arg Lys Val Arg Asp Leu  
 50 55 60  
 Gln Glu Ala Asp Leu Asp Leu Leu Arg Val Thr Leu Ser Ser Lys Pro  
 65 70 75 80  
 Gln Ala Leu Ala Thr Pro Asn Lys Glu Glu His Gly Lys Arg Lys Lys  
 85 90 95  
 Lys Gly Lys Gly Leu Gly Lys Lys Arg Asp Pro Cys Leu Arg Lys Tyr  
 100 105 110  
 Lys Asp Phe Cys Ile His Gly Glu Cys Lys Tyr Val Lys Glu Leu Arg  
 115 120 125  
 Ala Pro Ser Cys Ile Cys His Pro Gly Tyr His Gly Glu Arg Cys His  
 130 135 140  
 Gly Leu Ser Leu Pro Val Glu Asn Arg Leu Tyr Thr Tyr Asp His Thr  
 145 150 155 160  
 Thr Ile Leu Ala Val Val Ala Val Val Leu Ser Ser Val Cys Leu Leu  
 165 170 175  
 Val Ile Val Gly Leu Leu Met Phe Arg Tyr His Arg Arg Gly Gly Tyr  
 180 185 190  
 Asp Val Glu Asn Glu Glu Lys Val Lys Leu Gly Met Thr Asn Ser His  
 195 200 205

&lt;210&gt; 202

&lt;211&gt; 662

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 202  
 Met Arg Pro Gln Ile Leu Leu Leu Leu Ala Leu Leu Thr Leu Gly Leu  
 1 5 10 15  
 Ala Ala Gln His Gln Asp Lys Val Pro Cys Lys Met Val Asp Lys Lys  
 20 25 30  
 Val Ser Cys Gln Val Leu Gly Leu Leu Gln Val Pro Ser Val Leu Pro  
 35 40 45  
 Pro Asp Thr Glu Thr Leu Asp Leu Ser Gly Asn Gln Leu Arg Ser Ile  
 50 55 60  
 Leu Ala Ser Pro Leu Gly Phe Tyr Thr Ala Leu Arg His Leu Asp Leu  
 65 70 75 80  
 Ser Thr Asn Glu Ile Ser Phe Leu Gln Pro Gly Ala Phe Gln Ala Leu  
 85 90 95  
 Thr His Leu Glu His Leu Ser Leu Ala His Asn Arg Leu Ala Met Ala  
 100 105 110  
 Thr Ala Leu Ser Ala Gly Gly Leu Gly Pro Leu Pro Arg Val Thr Ser  
 115 120 125  
 Leu Asp Leu Ser Gly Asn Ser Leu Tyr Ser Gly Leu Leu Glu Arg Leu  
 130 135 140  
 Leu Gly Glu Ala Pro Ser Leu His Thr Leu Ser Leu Ala Glu Asn Ser  
 145 150 155 160  
 Leu Thr Arg Leu Thr Arg His Thr Phe Arg Asp Met Pro Ala Leu Glu  
 165 170 175  
 Gln Leu Asp Leu His Ser Asn Val Leu Met Asp Ile Glu Asp Gly Ala  
 180 185 190  
 Phe Glu Gly Leu Pro Arg Leu Thr His Leu Asn Leu Ser Arg Asn Ser  
 195 200 205  
 Leu Thr Cys Ile Ser Asp Phe Ser Leu Gln Gln Leu Arg Val Leu Asp  
 210 215 220  
 Leu Ser Cys Asn Ser Ile Glu Ala Phe Gln Thr Ala Ser Gln Pro Gln  
 225 230 235 240

Ala Glu Phe Gln Leu Thr Trp Leu Asp Leu Arg Glu Asn Lys Leu Leu  
 245 250 255  
 His Phe Pro Asp Leu Ala Ala Leu Pro Arg Leu Ile Tyr Leu Asn Leu  
 260 265 270  
 Ser Asn Asn Leu Ile Arg Leu Pro Thr Gly Pro Pro Gln Asp Ser Lys  
 275 280 285  
 Gly Ile His Ala Pro Ser Glu Gly Trp Ser Ala Leu Pro Leu Ser Ala  
 290 295 300  
 Pro Ser Gly Asn Ala Ser Gly Arg Pro Leu Ser Gln Leu Leu Asn Leu  
 305 310 315 320  
 Asp Leu Ser Tyr Asn Glu Ile Glu Leu Ile Pro Asp Ser Phe Leu Glu  
 325 330 335  
 His Leu Thr Ser Leu Cys Phe Leu Asn Leu Ser Arg Asn Cys Leu Arg  
 340 345 350  
 Thr Phe Glu Ala Arg Arg Leu Gly Ser Leu Pro Cys Leu Met Leu Leu  
 355 360 365  
 Asp Leu Ser His Asn Ala Leu Glu Thr Leu Glu Leu Gly Ala Arg Ala  
 370 375 380  
 Leu Gly Ser Leu Arg Thr Leu Leu Leu Gln Gly Asn Ala Leu Arg Asp  
 385 390 395 400  
 Leu Pro Pro Tyr Thr Phe Ala Asn Leu Ala Ser Leu Gln Arg Leu Asn  
 405 410 415  
 Leu Gln Gly Asn Arg Val Ser Pro Cys Gly Gly Pro Asp Glu Pro Gly  
 420 425 430  
 Pro Ser Gly Cys Val Ala Phe Ser Gly Ile Thr Ser Leu Arg Ser Leu  
 435 440 445  
 Ser Leu Val Asp Asn Glu Ile Glu Leu Leu Arg Ala Gly Ala Phe Leu  
 450 455 460  
 His Thr Pro Leu Thr Glu Leu Asp Leu Ser Ser Asn Pro Gly Leu Glu  
 465 470 475 480  
 Val Ala Thr Gly Ala Leu Gly Gly Leu Glu Ala Ser Leu Glu Val Leu  
 485 490 495  
 Ala Leu Gln Gly Asn Gly Leu Met Val Leu Gln Val Asp Leu Pro Cys  
 500 505 510  
 Phe Ile Cys Leu Lys Arg Leu Asn Leu Ala Glu Asn Arg Leu Ser His  
 515 520 525  
 Leu Pro Ala Trp Thr Gln Ala Val Ser Leu Glu Val Leu Asp Leu Arg  
 530 535 540  
 Asn Asn Ser Phe Ser Leu Leu Pro Gly Ser Ala Met Gly Gly Leu Glu  
 545 550 555 560  
 Thr Ser Leu Arg Arg Leu Tyr Leu Gln Gly Asn Pro Leu Ser Cys Cys  
 565 570 575  
 Gly Asn Gly Trp Leu Ala Ala Gln Leu His Gln Gly Arg Val Asp Val  
 580 585 590  
 Asp Ala Thr Gln Asp Leu Ile Cys Arg Phe Ser Ser Gln Glu Glu Val  
 595 600 605  
 Ser Leu Ser His Val Arg Pro Glu Asp Cys Glu Lys Gly Gly Leu Lys  
 610 615 620  
 Asn Ile Asn Leu Ile Ile Ile Leu Thr Phe Ile Leu Val Ser Ala Ile  
 625 630 635 640  
 Leu Leu Thr Thr Leu Ala Ala Cys Cys Cys Val Arg Arg Gln Lys Phe  
 645 650 655  
 Asn Gln Gln Tyr Lys Ala  
 660

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&lt;210&gt; 203

&lt;211&gt; 1036

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 203

Met Gln Pro Glu Glu Gly Thr Gly Trp Leu Leu Glu Leu Leu Ser Glu  
 1 5 10 15  
 Val Gln Leu Gln Gln Tyr Phe Leu Arg Leu Arg Asp Asp Leu Asn Val  
 20 25 30  
 Thr Arg Leu Ser His Phe Glu Tyr Val Lys Asn Glu Asp Leu Glu Lys  
 35 40 45  
 Ile Gly Met Gly Arg Pro Gly Gln Arg Arg Leu Trp Glu Ala Val Lys  
 50 55 60  
 Arg Arg Lys Ala Leu Cys Lys Arg Lys Ser Trp Met Ser Lys Val Phe  
 65 70 75 80  
 Ser Gly Lys Arg Leu Glu Ala Glu Phe Pro Pro His His Ser Gln Ser  
 85 90 95  
 Thr Phe Arg Lys Thr Ser Pro Ala Pro Gly Gly Pro Ala Gly Glu Gly  
 100 105 110  
 Pro Leu Gln Ser Leu Thr Cys Leu Ile Gly Glu Lys Asp Leu Arg Leu  
 115 120 125  
 Leu Glu Lys Leu Gly Asp Gly Ser Phe Gly Val Val Arg Arg Gly Glu  
 130 135 140  
 Trp Asp Ala Pro Ser Gly Lys Thr Val Ser Val Ala Val Lys Cys Leu  
 145 150 155 160  
 Lys Pro Asp Val Leu Ser Gln Pro Glu Ala Met Asp Asp Phe Ile Arg  
 165 170 175  
 Glu Val Asn Ala Met His Ser Leu Asp His Arg Asn Leu Ile Arg Leu  
 180 185 190  
 Tyr Gly Val Val Leu Thr Pro Pro Met Lys Met Val Thr Glu Leu Ala  
 195 200 205  
 Pro Leu Gly Ser Leu Leu Asp Arg Leu Arg Lys His Gln Gly His Phe  
 210 215 220  
 Leu Leu Gly Thr Leu Ser Arg Tyr Ala Val Gln Val Ala Glu Gly Met  
 225 230 235 240  
 Gly Tyr Leu Glu Ser Lys Arg Phe Ile His Arg Asp Leu Ala Ala Arg  
 245 250 255  
 Asn Leu Leu Leu Ala Thr Arg Asp Leu Val Lys Ile Gly Asp Phe Gly  
 260 265 270  
 Leu Met Arg Ala Leu Pro Gln Asn Asp Asp His Tyr Val Met Gln Glu  
 275 280 285  
 His Arg Lys Val Pro Phe Ala Trp Cys Ala Pro Glu Ser Leu Lys Thr  
 290 295 300  
 Arg Thr Phe Ser His Ala Ser Asp Thr Trp Met Phe Gly Val Thr Leu  
 305 310 315 320  
 Trp Glu Met Phe Thr Tyr Gly Gln Glu Pro Trp Ile Gly Leu Asn Gly  
 325 330 335  
 Ser Gln Ile Leu His Lys Ile Asp Lys Glu Gly Glu Arg Leu Pro Arg  
 340 345 350  
 Pro Glu Asp Cys Pro Gln Asp Ile Tyr Asn Val Met Val Gln Cys Trp  
 355 360 365  
 Ala His Lys Pro Glu Asp Arg Pro Thr Phe Val Ala Leu Arg Asp Phe  
 370 375 380  
 Leu Leu Glu Ala Gln Pro Thr Asp Met Arg Ala Leu Gln Asp Phe Glu  
 385 390 395 400

Glu Pro Asp Lys Leu His Ile Gln Met Asn Asp Val Ile Thr Val Ile  
 405 410 415  
 Glu Gly Arg Ala Glu Asn Tyr Trp Trp Arg Gly Gln Asn Thr Arg Thr  
 420 425 430  
 Leu Cys Val Gly Pro Phe Pro Arg Asn Val Val Thr Ser Val Ala Gly  
 435 440 445  
 Leu Ser Ala Gln Asp Ile Ser Gln Pro Leu Gln Asn Ser Phe Ile His  
 450 455 460  
 Thr Gly His Gly Asp Ser Asp Pro Arg His Cys Trp Gly Phe Pro Asp  
 465 470 475 480  
 Arg Ile Asp Glu Leu Tyr Leu Gly Asn Pro Met Asp Pro Pro Asp Leu  
 485 490 495  
 Leu Ser Val Glu Leu Ser Thr Ser Arg Pro Pro Gln His Leu Gly Gly  
 500 505 510  
 Val Lys Lys Pro Thr Tyr Asp Pro Val Ser Glu Asp Gln Asp Pro Leu  
 515 520 525  
 Ser Ser Asp Phe Lys Arg Leu Gly Leu Arg Lys Pro Gly Leu Pro Arg  
 530 535 540  
 Gly Leu Trp Leu Ala Lys Pro Ser Ala Arg Val Pro Gly Thr Lys Ala  
 545 550 555 560  
 Ser Arg Gly Ser Gly Ala Glu Val Thr Leu Ile Asp Phe Gly Glu Glu  
 565 570 575  
 Pro Val Val Pro Ala Leu Arg Pro Cys Pro Pro Ser Leu Ala Gln Leu  
 580 585 590  
 Ala Met Asp Ala Cys Ser Leu Leu Asp Glu Thr Pro Pro Gln Ser Pro  
 595 600 605  
 Thr Arg Ala Leu Pro Arg Pro Leu His Pro Thr Pro Val Val Asp Trp  
 610 615 620  
 Asp Ala Arg Pro Leu Pro Pro Pro Pro Ala Tyr Asp Asp Val Ala Gln  
 625 630 635 640  
 Asp Glu Asp Asp Phe Glu Ile Cys Ser Ile Asn Ser Thr Leu Val Gly  
 645 650 655  
 Ala Gly Val Pro Ala Gly Pro Ser Gln Gly Gln Thr Asn Tyr Ala Phe  
 660 665 670  
 Val Pro Glu Gln Ala Arg Pro Pro Pro Pro Leu Glu Asp Asn Leu Phe  
 675 680 685  
 Leu Pro Pro Gln Gly Gly Gly Lys Pro Pro Ser Ser Ala Gln Thr Ala  
 690 695 700  
 Glu Ile Phe Gln Ala Leu Gln Gln Glu Cys Met Arg Gln Leu Gln Ala  
 705 710 715 720  
 Pro Gly Ser Pro Ala Pro Ser Pro Ser Pro Gly Gly Asp Asp Lys Pro  
 725 730 735  
 Gln Val Pro Pro Arg Val Pro Ile Pro Pro Arg Pro Thr Arg Pro His  
 740 745 750  
 Val Gln Leu Ser Pro Ala Pro Pro Gly Glu Glu Glu Thr Ser Gln Trp  
 755 760 765  
 Pro Gly Pro Ala Ser Pro Pro Arg Val Pro Pro Arg Glu Pro Leu Ser  
 770 775 780  
 Pro Gln Gly Ser Arg Thr Pro Ser Pro Leu Val Pro Pro Gly Ser Ser  
 785 790 795 800  
 Pro Leu Pro Pro Arg Leu Ser Ser Ser Pro Gly Lys Thr Met Pro Thr  
 805 810 815  
 Thr Gln Ser Phe Ala Ser Asp Pro Lys Tyr Ala Thr Pro Gln Val Ile  
 820 825 830  
 Gln Ala Pro Gly Ala Gly Gly Pro Cys Ile Leu Pro Ile Val Arg Asp  
 835 840 845  
 Gly Lys Lys Val Ser Ser Thr His Tyr Tyr Leu Leu Pro Glu Arg Pro  
 850 855 860  
 Ser Tyr Leu Glu Arg Tyr Gln Arg Phe Leu Arg Glu Ala Gln Ser Pro  
 865 870 875 880  
 Glu Glu Pro Thr Pro Leu Pro Val Pro Leu Leu Leu Pro Pro Pro Ser  
 885 890 895

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Thr Pro Ala Pro Ala Ala Pro Thr Ala Thr Val Arg Pro Met Pro Gln  
 900 905 910  
 Ala Ala Leu Asp Pro Lys Ala Asn Phe Ser Thr Asn Asn Ser Asn Pro  
 915 920 925  
 Gly Ala Arg Pro Pro Pro Pro Arg Ala Thr Ala Arg Leu Pro Gln Arg  
 930 935 940  
 Gly Cys Pro Gly Asp Gly Pro Glu Ala Gly Arg Pro Ala Asp Lys Ile  
 945 950 955 960  
 Gln Met Ala Met Val His Gly Val Thr Thr Glu Glu Cys Gln Ala Ala  
 965 970 975  
 Leu Gln Cys His Gly Trp Ser Val Gln Arg Ala Ala Gln Tyr Leu Lys  
 980 985 990  
 Val Glu Gln Leu Phe Gly Leu Gly Leu Arg Pro Arg Gly Glu Cys His  
 995 1000 1005  
 Lys Val Leu Glu Met Phe Asp Trp Asn Leu Glu Gln Ala Gly Cys  
 1010 1015 1020  
 His Leu Leu Gly Ser Trp Gly Pro Ala His His Lys Arg  
 1025 1030 1035  
 <210> 204  
 <211> 364  
 <212> PRT  
 <213> Homo sapiens

<400> 204  
 Met Ala Ala Ile Ser Thr Ser Ile Pro Val Ile Ser Gln Pro Gln Phe  
 1 5 10 15  
 Thr Ala Met Asn Glu Pro Gln Cys Phe Tyr Asn Glu Ser Ile Ala Phe  
 20 25 30  
 Phe Tyr Asn Arg Ser Gly Lys His Leu Ala Thr Glu Trp Asn Thr Val  
 35 40 45  
 Ser Lys Leu Val Met Gly Leu Gly Ile Thr Val Cys Ile Phe Ile Met  
 50 55 60  
 Leu Ala Asn Leu Leu Val Met Val Ala Ile Tyr Val Asn Arg Arg Phe  
 65 70 75 80  
 His Phe Pro Ile Tyr Tyr Leu Met Ala Asn Leu Ala Ala Ala Asp Phe  
 85 90 95  
 Phe Ala Gly Leu Ala Tyr Phe Tyr Leu Met Phe Asn Thr Gly Pro Asn  
 100 105 110  
 Thr Arg Arg Leu Thr Val Ser Thr Trp Leu Leu Arg Gln Gly Leu Ile  
 115 120 125  
 Asp Thr Ser Leu Thr Ala Ser Val Ala Asn Leu Leu Ala Ile Ala Ile  
 130 135 140  
 Glu Arg His Ile Thr Val Phe Arg Met Gln Leu His Thr Arg Met Ser  
 145 150 155 160  
 Asn Arg Arg Val Val Val Ile Val Val Ile Trp Thr Met Ala Ile  
 165 170 175  
 Val Met Gly Ala Ile Pro Ser Val Gly Trp Asn Cys Ile Cys Asp Ile  
 180 185 190  
 Glu Asn Cys Ser Asn Met Ala Pro Leu Tyr Ser Asp Ser Tyr Leu Val  
 195 200 205  
 Phe Trp Ala Ile Phe Asn Leu Val Thr Phe Val Val Met Val Val Leu  
 210 215 220  
 Tyr Ala His Ile Phe Gly Tyr Val Arg Gln Arg Thr Met Arg Met Ser  
 225 230 235 240  
 Arg His Ser Ser Gly Pro Arg Arg Asn Arg Asp Thr Met Met Ser Leu  
 245 250 255

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Leu Lys Thr Val Val Ile Val Leu Gly Ala Phe Ile Ile Cys Trp Thr  
 260 265 270  
 Pro Gly Leu Val Leu Leu Leu Leu Asp Val Cys Cys Pro Gln Cys Asp  
 275 280 285  
 Val Leu Ala Tyr Glu Lys Phe Phe Leu Leu Leu Ala Glu Phe Asn Ser  
 290 295 300  
 Ala Met Asn Pro Ile Ile Tyr Ser Tyr Arg Asp Lys Glu Met Ser Ala  
 305 310 315 320  
 Thr Phe Arg Gln Ile Leu Cys Cys Gln Arg Ser Glu Asn Pro Thr Gly  
 325 330 335  
 Pro Thr Glu Gly Ser Asp Arg Ser Ala Ser Ser Leu Asn His Thr Ile  
 340 345 350  
 Leu Ala Gly Val His Ser Asn Asp His Ser Val Val  
 355 360  
 <210> 205  
 <211> 164  
 <212> PRT  
 <213> Homo sapiens

<400> 205  
 Met Ala Ser Pro His Gln Glu Pro Lys Pro Gly Asp Leu Ile Glu Ile  
 1 5 10 15  
 Phe Arg Leu Gly Tyr Glu His Trp Ala Leu Tyr Ile Gly Asp Gly Tyr  
 20 25 30  
 Val Ile His Leu Ala Pro Pro Ser Glu Tyr Pro Gly Ala Gly Ser Ser  
 35 40 45  
 Ser Val Phe Ser Val Leu Ser Asn Ser Ala Glu Val Lys Arg Gly Arg  
 50 55 60  
 Leu Glu Asp Val Val Gly Gly Cys Cys Tyr Arg Val Asn Asn Ser Leu  
 65 70 75 80  
 Asp His Glu Tyr Gln Pro Arg Pro Val Glu Val Ile Ile Ser Ser Ala  
 85 90 95  
 Lys Glu Met Val Gly Gln Lys Met Lys Tyr Ser Ile Val Ser Arg Asn  
 100 105 110  
 Cys Glu His Phe Val Ala Gln Leu Arg Tyr Gly Lys Ser Arg Cys Lys  
 115 120 125  
 Gln Val Glu Lys Ala Lys Val Glu Val Gly Val Ala Thr Ala Leu Gly  
 130 135 140  
 Ile Leu Val Val Ala Gly Cys Ser Phe Ala Ile Arg Arg Tyr Gln Lys  
 145 150 155 160  
 Lys Ala Thr Ala

<210> 206  
 <211> 323  
 <212> PRT  
 <213> Homo sapiens

<400> 206  
 Met Tyr His Asn Ser Ser Gln Lys Arg His Trp Thr Phe Ser Ser Glu  
 1 5 10 15  
 Glu Gln Leu Ala Arg Leu Arg Ala Asp Ala Asn Arg Lys Phe Arg Cys  
 20 25 30



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Lys Ala Val Ala Asn Gly Lys Val Leu Pro Asn Asp Pro Val Phe Leu  
 35 40 45  
 Glu Pro His Glu Glu Met Thr Leu Cys Lys Tyr Tyr Glu Lys Arg Leu  
 50 55 60  
 Leu Glu Phe Cys Ser Val Phe Lys Pro Ala Met Pro Arg Ser Val Val  
 65 70 75 80  
 Gly Thr Ala Cys Met Tyr Phe Lys Arg Phe Tyr Leu Asn Asn Ser Val  
 85 90 95  
 Met Glu Tyr His Pro Arg Ile Ile Met Leu Thr Cys Ala Phe Leu Ala  
 100 105 110  
 Cys Lys Val Asp Glu Phe Asn Val Ser Ser Pro Gln Phe Val Gly Asn  
 115 120 125  
 Leu Arg Glu Ser Pro Leu Gly Gln Glu Lys Ala Leu Glu Gln Ile Leu  
 130 135 140  
 Glu Tyr Glu Leu Leu Leu Ile Gln Gln Leu Asn Phe His Leu Ile Val  
 145 150 155 160  
 His Asn Pro Tyr Arg Pro Phe Glu Gly Phe Leu Ile Asp Leu Lys Thr  
 165 170 175  
 Arg Tyr Pro Ile Leu Glu Asn Pro Glu Ile Leu Arg Lys Thr Ala Asp  
 180 185 190  
 Asp Phe Leu Asn Arg Ile Ala Leu Thr Asp Ala Tyr Leu Leu Tyr Thr  
 195 200 205  
 Pro Ser Gln Ile Ala Leu Thr Ala Ile Leu Ser Ser Ala Ser Arg Ala  
 210 215 220  
 Gly Ile Thr Met Glu Ser Tyr Leu Ser Glu Ser Leu Met Leu Lys Glu  
 225 230 235 240  
 Asn Arg Thr Cys Leu Ser Gln Leu Leu Asp Ile Met Lys Ser Met Arg  
 245 250 255  
 Asn Leu Val Lys Lys Tyr Glu Pro Pro Arg Ser Glu Glu Val Ala Val  
 260 265 270  
 Leu Lys Gln Lys Leu Glu Arg Cys His Ser Ala Glu Leu Ala Leu Asn  
 275 280 285  
 Val Ile Thr Lys Lys Arg Lys Gly Tyr Glu Asp Asp Tyr Val Ser  
 290 295 300  
 Lys Lys Ser Lys His Glu Glu Glu Glu Trp Thr Asp Asp Asp Leu Val  
 305 310 315 320  
 Glu Ser Leu

&lt;210&gt; 207

&lt;211&gt; 710

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 207  
 Met Leu Ser Phe Gln Tyr Pro Asp Val Tyr Arg Asp Glu Thr Ala Val  
 1 5 10 15  
 Gln Asp Tyr His Gly His Lys Ile Cys Asp Pro Tyr Ala Trp Leu Glu  
 20 25 30  
 Asp Pro Asp Ser Glu Gln Thr Lys Ala Phe Val Glu Ala Gln Asn Lys  
 35 40 45  
 Ile Thr Val Pro Phe Leu Glu Gln Cys Pro Ile Arg Gly Leu Tyr Lys  
 50 55 60  
 Glu Arg Met Thr Glu Leu Tyr Asp Tyr Pro Lys Tyr Ser Cys His Phe  
 65 70 75 80  
 Lys Lys Gly Lys Arg Tyr Phe Tyr Phe Tyr Asn Thr Gly Leu Gln Asn  
 85 90 95

Gln Arg Val Leu Tyr Val Gln Asp Ser Leu Glu Gly Glu Ala Arg Val  
 100 105 110  
 Phe Leu Asp Pro Asn Ile Leu Ser Asp Asp Gly Thr Val Ala Leu Arg  
 115 120 125  
 Gly Tyr Ala Phe Ser Glu Asp Gly Glu Tyr Phe Ala Tyr Gly Leu Ser  
 130 135 140  
 Ala Ser Gly Ser Asp Trp Val Thr Ile Lys Phe Met Lys Val Asp Gly  
 145 150 155 160  
 Ala Lys Glu Leu Pro Asp Val Leu Glu Arg Val Lys Phe Ser Cys Met  
 165 170 175  
 Ala Trp Thr His Asp Gly Lys Gly Met Phe Tyr Asn Ser Tyr Pro Gln  
 180 185 190  
 Gln Asp Gly Lys Ser Asp Gly Thr Glu Thr Ser Thr Asn Leu His Gln  
 195 200 205  
 Lys Leu Tyr Tyr His Val Leu Gly Thr Asp Gln Ser Glu Asp Ile Leu  
 210 215 220  
 Cys Ala Glu Phe Pro Asp Glu Pro Lys Trp Met Gly Gly Ala Glu Leu  
 225 230 235 240  
 Ser Asp Asp Gly Arg Tyr Val Leu Leu Ser Ile Arg Glu Gly Cys Asp  
 245 250 255  
 Pro Val Asn Arg Leu Trp Tyr Cys Asp Leu Gln Gln Glu Ser Ser Gly  
 260 265 270  
 Ile Ala Gly Ile Leu Lys Trp Val Lys Leu Ile Asp Asn Phe Glu Gly  
 275 280 285  
 Glu Tyr Asp Tyr Val Thr Asn Glu Gly Ala Val Phe Thr Phe Lys Thr  
 290 295 300  
 Asn Arg Gln Ser Pro Asn Tyr Arg Val Ile Asn Ile Asp Phe Arg Asp  
 305 310 315 320  
 Pro Glu Glu Ser Lys Trp Lys Val Leu Val Pro Glu His Glu Lys Asp  
 325 330 335  
 Val Leu Glu Trp Ile Ala Cys Val Arg Ser Asn Phe Leu Val Leu Cys  
 340 345 350  
 Tyr Leu His Asp Val Lys Asn Ile Leu Gln Leu His Asp Leu Thr Thr  
 355 360 365  
 Gly Ala Leu Leu Lys Thr Phe Pro Leu Asp Val Gly Ser Ile Val Gly  
 370 375 380  
 Tyr Ser Gly Gln Lys Lys Asp Thr Glu Ile Phe Tyr Gln Phe Thr Ser  
 385 390 395 400  
 Phe Leu Ser Pro Gly Ile Ile Tyr His Cys Asp Leu Thr Lys Glu  
 405 410 415  
 Leu Glu Pro Arg Val Phe Arg Glu Val Thr Val Lys Gly Ile Asp Ala  
 420 425 430  
 Ser Asp Tyr Gln Thr Val Gln Ile Phe Tyr Pro Ser Lys Asp Gly Thr  
 435 440 445  
 Lys Ile Pro Met Phe Ile Val His Lys Lys Ser Ile Lys Leu Asp Gly  
 450 455 460  
 Ser His Pro Ala Phe Leu Tyr Gly Tyr Gly Gly Phe Asn Ile Ser Ile  
 465 470 475 480  
 Thr Pro Asn Tyr Ser Val Ser Arg Leu Ile Phe Val Arg His Met Gly  
 485 490 495  
 Gly Ile Leu Ala Val Ala Asn Ile Arg Gly Gly Glu Tyr Gly Glu  
 500 505 510  
 Thr Trp His Lys Gly Gly Ile Leu Ala Asn Lys Gln Asn Cys Phe Asp  
 515 520 525  
 Asp Phe Gln Cys Ala Ala Glu Tyr Leu Ile Lys Glu Gly Tyr Thr Ser  
 530 535 540  
 Pro Lys Arg Leu Thr Ile Asn Gly Gly Ser Asn Gly Gly Leu Leu Val  
 545 550 555 560  
 Ala Ala Cys Ala Asn Gln Arg Pro Asp Leu Phe Gly Cys Val Ile Ala  
 565 570 575  
 Gln Val Gly Val Met Asp Met Leu Lys Phe His Lys Tyr Thr Ile Gly  
 580 585 590

His Ala Trp Thr Thr Asp Tyr Gly Cys Ser Asp Ser Lys Gln His Phe  
 595 600 605  
 Glu Trp Leu Val Lys Tyr Ser Pro Leu His Asn Val Lys Leu Pro Glu  
 610 615 620  
 Ala Asp Asp Ile Gln Tyr Pro Ser Met Leu Leu Thr Ala Asp His  
 625 630 635 640  
 Asp Asp Arg Val Val Pro Leu His Ser Leu Lys Phe Ile Ala Thr Leu  
 645 650 655  
 Gln Tyr Ile Val Gly Arg Ser Arg Lys Gln Ser Asn Pro Leu Leu Ile  
 660 665 670  
 His Val Asp Thr Lys Ala Gly His Gly Ala Gly Lys Pro Thr Ala Lys  
 675 680 685  
 Val Ile Glu Glu Val Ser Asp Met Phe Ala Phe Ile Ala Arg Cys Leu  
 690 695 700  
 Asn Val Asp Trp Ile Pro  
 705 710  
 <210> 208  
 <211> 1806  
 <212> PRT  
 <213> Homo sapiens

<400> 208  
 Met Glu Pro Trp Ser Ser Arg Trp Lys Thr Lys Arg Trp Leu Trp Asp  
 1 5 10 15  
 Phe Thr Val Thr Thr Leu Ala Leu Thr Phe Leu Phe Gln Ala Arg Glu  
 20 25 30  
 Val Arg Gly Ala Ala Pro Val Asp Val Leu Lys Ala Leu Asp Phe His  
 35 40 45  
 Asn Ser Pro Glu Gly Ile Ser Lys Thr Thr Gly Phe Cys Thr Asn Arg  
 50 55 60  
 Lys Asn Ser Lys Gly Ser Asp Thr Ala Tyr Arg Val Ser Lys Gln Ala  
 65 70 75 80  
 Gln Leu Ser Ala Pro Thr Lys Gln Leu Phe Pro Gly Gly Thr Phe Pro  
 85 90 95  
 Glu Asp Phe Ser Ile Leu Phe Thr Val Lys Pro Lys Lys Gly Ile Gln  
 100 105 110  
 Ser Phe Leu Leu Ser Ile Tyr Asn Glu His Gly Ile Gln Gln Ile Gly  
 115 120 125  
 Val Glu Val Gly Arg Ser Pro Val Phe Leu Phe Glu Asp His Thr Gly  
 130 135 140  
 Lys Pro Ala Pro Glu Asp Tyr Pro Leu Phe Arg Thr Val Asn Ile Ala  
 145 150 155 160  
 Asp Gly Lys Trp His Arg Val Ala Ile Ser Val Glu Lys Lys Thr Val  
 165 170 175  
 Thr Met Ile Val Asp Cys Lys Lys Lys Thr Thr Lys Pro Leu Asp Arg  
 180 185 190  
 Ser Glu Arg Ala Ile Val Asp Thr Asn Gly Ile Thr Val Phe Gly Thr  
 195 200 205  
 Arg Ile Leu Asp Glu Glu Val Phe Glu Gly Asp Ile Gln Gln Phe Leu  
 210 215 220  
 Ile Thr Gly Asp Pro Lys Ala Ala Tyr Asp Tyr Cys Glu His Tyr Ser  
 225 230 235 240  
 Pro Asp Cys Asp Ser Ser Ala Pro Lys Ala Ala Gln Ala Gln Glu Pro  
 245 250 255  
 Gln Ile Asp Glu Tyr Ala Pro Glu Asp Ile Ile Glu Tyr Asp Tyr Glu  
 260 265 270

Tyr	Gly	Glu	Ala	Glu	Tyr	Lys	Glu	Ala	Glu	Ser	Val	Thr	Glu	Gly	Pro
		275					280					285			
Thr	Val	Thr	Glu	Glu	Thr	Ile	Ala	Gln	Thr	Glu	Ala	Asn	Ile	Val	Asp
	290					295					300				
Asp	Phe	Gln	Glu	Tyr	Asn	Tyr	Gly	Thr	Met	Glu	Ser	Tyr	Gln	Thr	Glu
305					310					315					320
Ala	Pro	Arg	His	Val	Ser	Gly	Thr	Asn	Glu	Pro	Asn	Pro	Val	Glu	Glu
				325					330					335	
Ile	Phe	Thr	Glu	Glu	Tyr	Leu	Thr	Gly	Glu	Asp	Tyr	Asp	Ser	Gln	Arg
			340					345					350		
Lys	Asn	Ser	Glu	Asp	Thr	Leu	Tyr	Glu	Asn	Lys	Glu	Ile	Asp	Gly	Arg
		355				360						365			
Asp	Ser	Asp	Leu	Leu	Val	Asp	Gly	Asp	Leu	Gly	Glu	Tyr	Asp	Phe	Tyr
	370					375					380				
Glu	Tyr	Lys	Glu	Tyr	Glu	Asp	Lys	Pro	Thr	Ser	Pro	Pro	Asn	Glu	Glu
385					390					395					400
Phe	Gly	Pro	Gly	Val	Pro	Ala	Glu	Thr	Asp	Ile	Thr	Glu	Thr	Ser	Ile
				405					410					415	
Asn	Gly	His	Gly	Ala	Tyr	Gly	Glu	Lys	Gly	Gln	Lys	Gly	Glu	Pro	Ala
			420					425					430		
Val	Val	Glu	Pro	Gly	Met	Leu	Val	Glu	Gly	Pro	Pro	Gly	Pro	Ala	Gly
		435				440						445			
Pro	Ala	Gly	Ile	Met	Gly	Pro	Pro	Gly	Leu	Gln	Gly	Pro	Thr	Gly	Pro
	450				455						460				
Pro	Gly	Asp	Pro	Gly	Asp	Arg	Gly	Pro	Pro	Gly	Arg	Pro	Gly	Leu	Pro
465					470					475				480	
Gly	Ala	Asp	Gly	Leu	Pro	Gly	Pro	Pro	Gly	Thr	Met	Leu	Met	Leu	Pro
				485					490					495	
Phe	Arg	Tyr	Gly	Gly	Asp	Gly	Ser	Lys	Gly	Pro	Thr	Ile	Ser	Ala	Gln
			500					505					510		
Glu	Ala	Gln	Ala	Gln	Ala	Ile	Leu	Gln	Gln	Ala	Arg	Ile	Ala	Leu	Arg
		515					520					525			
Gly	Pro	Pro	Gly	Pro	Met	Gly	Leu	Thr	Gly	Arg	Pro	Gly	Pro	Val	Gly
	530					535					540				
Gly	Pro	Gly	Ser	Ser	Gly	Ala	Lys	Gly	Glu	Ser	Gly	Asp	Pro	Gly	Pro
545					550					555					560
Gln	Gly	Pro	Arg	Gly	Val	Gln	Gly	Pro	Pro	Gly	Pro	Thr	Gly	Lys	Pro
				565					570					575	
Gly	Lys	Arg	Gly	Arg	Pro	Gly	Ala	Asp	Gly	Gly	Arg	Gly	Met	Pro	Gly
			580					585					590		
Glu	Pro	Gly	Ala	Lys	Gly	Asp	Arg	Gly	Phe	Asp	Gly	Leu	Pro	Gly	Leu
		595					600					605			
Pro	Gly	Asp	Lys	Gly	His	Arg	Gly	Glu	Arg	Gly	Pro	Gln	Gly	Pro	Pro
	610					615					620				
Gly	Pro	Pro	Gly	Asp	Asp	Gly	Met	Arg	Gly	Glu	Asp	Gly	Glu	Ile	Gly
625					630					635					640
Pro	Arg	Gly	Leu	Pro	Gly	Glu	Ala	Gly	Pro	Arg	Gly	Leu	Leu	Gly	Pro
				645					650					655	
Arg	Gly	Thr	Pro	Gly	Ala	Pro	Gly	Gln	Pro	Gly	Met	Ala	Gly	Val	Asp
			660					665					670		
Gly	Pro	Pro	Gly	Pro	Lys	Gly	Asn	Met	Gly	Pro	Gln	Gly	Glu	Pro	Gly
		675					680					685			
Pro	Pro	Gly	Gln	Gln	Gly	Asn	Pro	Gly	Pro	Gln	Gly	Leu	Pro	Gly	Pro
	690					695					700				
Gln	Gly	Pro	Ile	Gly	Pro	Pro	Gly	Glu	Lys	Gly	Pro	Gln	Gly	Lys	Pro
705					710					715					720
Gly	Leu	Ala	Gly	Leu	Pro	Gly	Ala	Asp	Gly	Pro	Pro	Gly	His	Pro	Gly
				725					730					735	
Lys	Glu	Gly	Gln	Ser	Gly	Glu	Lys	Gly	Ala	Leu	Gly	Pro	Pro	Gly	Pro
			740					745					750		
Gln	Gly	Pro	Ile	Gly	Tyr	Pro	Gly	Pro	Arg	Gly	Val	Lys	Gly	Ala	Asp
		755					760						765		

Gly Val Arg Gly Leu Lys Gly Ser Lys Gly Glu Lys Gly Glu Asp Gly  
 770 775 780  
 Phe Pro Gly Phe Lys Gly Asp Met Gly Leu Lys Gly Asp Arg Gly Glu  
 785 790 795 800  
 Val Gly Gln Ile Gly Pro Arg Gly Glu Asp Gly Pro Glu Gly Pro Lys  
 805 810 815  
 Gly Arg Ala Gly Pro Thr Gly Asp Pro Gly Pro Ser Gly Gln Ala Gly  
 820 825 830  
 Glu Lys Gly Lys Leu Gly Val Pro Gly Leu Pro Gly Tyr Pro Gly Arg  
 835 840 845  
 Gln Gly Pro Lys Gly Ser Thr Gly Phe Pro Gly Phe Pro Gly Ala Asn  
 850 855 860  
 Gly Glu Lys Gly Ala Arg Gly Val Ala Gly Lys Pro Gly Pro Arg Gly  
 865 870 875 880  
 Gln Arg Gly Pro Thr Gly Pro Arg Gly Ser Arg Gly Ala Arg Gly Pro  
 885 890 895  
 Thr Gly Lys Pro Gly Pro Lys Gly Thr Ser Gly Gly Asp Gly Pro Pro  
 900 905 910  
 Gly Pro Pro Gly Glu Arg Gly Pro Gln Gly Pro Gln Gly Pro Val Gly  
 915 920 925  
 Phe Pro Gly Pro Lys Gly Pro Pro Gly Pro Pro Gly Arg Met Gly Cys  
 930 935 940  
 Pro Gly His Pro Gly Gln Arg Gly Glu Thr Gly Phe Gln Gly Lys Thr  
 945 950 955 960  
 Gly Pro Pro Gly Pro Gly Gly Val Val Gly Pro Gln Gly Pro Thr Gly  
 965 970 975  
 Glu Thr Gly Pro Ile Gly Glu Arg Gly His Pro Gly Pro Pro Gly Pro  
 980 985 990  
 Pro Gly Glu Gln Gly Leu Pro Gly Ala Ala Gly Lys Glu Gly Ala Lys  
 995 1000 1005  
 Gly Asp Pro Gly Pro Gln Gly Ile Ser Gly Lys Asp Gly Pro Ala  
 1010 1015 1020  
 Gly Leu Arg Gly Phe Pro Gly Glu Arg Gly Leu Pro Gly Ala Gln  
 1025 1030 1035  
 Gly Ala Pro Gly Leu Lys Gly Gly Glu Gly Pro Gln Gly Pro Pro  
 1040 1045 1050  
 Gly Pro Val Gly Ser Pro Gly Glu Arg Gly Ser Ala Gly Thr Ala  
 1055 1060 1065  
 Gly Pro Ile Gly Leu Pro Gly Arg Pro Gly Pro Gln Gly Pro Pro  
 1070 1075 1080  
 Gly Pro Ala Gly Glu Lys Gly Ala Pro Gly Glu Lys Gly Pro Gln  
 1085 1090 1095  
 Gly Pro Ala Gly Arg Asp Gly Val Gln Gly Pro Val Gly Leu Pro  
 1100 1105 1110  
 Gly Pro Ala Gly Pro Ala Gly Ser Pro Gly Glu Asp Gly Asp Lys  
 1115 1120 1125  
 Gly Glu Ile Gly Glu Pro Gly Gln Lys Gly Ser Lys Gly Asp Lys  
 1130 1135 1140  
 Gly Glu Asn Gly Pro Pro Gly Pro Pro Gly Leu Gln Gly Pro Val  
 1145 1150 1155  
 Gly Ala Pro Gly Ile Ala Gly Gly Asp Gly Glu Pro Gly Pro Arg  
 1160 1165 1170  
 Gly Gln Gln Gly Met Phe Gly Gln Lys Gly Asp Glu Gly Ala Arg  
 1175 1180 1185  
 Gly Phe Pro Gly Pro Pro Gly Pro Ile Gly Leu Gln Gly Leu Pro  
 1190 1195 1200  
 Gly Pro Pro Gly Glu Lys Gly Glu Asn Gly Asp Val Gly Pro Trp  
 1205 1210 1215  
 Gly Pro Pro Gly Pro Pro Gly Pro Arg Gly Pro Gln Gly Pro Asn  
 1220 1225 1230  
 Gly Ala Asp Gly Pro Gln Gly Pro Pro Gly Ser Val Gly Ser Val  
 1235 1240 1245

Gly	Gly	Val	Gly	Glu	Lys	Gly	Glu	Pro	Gly	Glu	Ala	Gly	Asn	Pro
1250	1255					1255					1260			
Gly	Pro	Pro	Gly	Glu	Ala	Gly	Val	Gly	Gly	Pro	Lys	Gly	Glu	Arg
1265	1270					1270					1275			
Gly	Glu	Lys	Gly	Glu	Ala	Gly	Pro	Pro	Gly	Ala	Ala	Gly	Pro	Pro
1280	1285					1285					1290			
Gly	Ala	Lys	Gly	Pro	Pro	Gly	Asp	Asp	Gly	Pro	Lys	Gly	Asn	Pro
1295	1300					1300					1305			
Gly	Pro	Val	Gly	Phe	Pro	Gly	Asp	Pro	Gly	Pro	Pro	Gly	Glu	Leu
1310	1315					1315					1320			
Gly	Pro	Ala	Gly	Gln	Asp	Gly	Val	Gly	Gly	Asp	Lys	Gly	Glu	Asp
1325	1330					1330					1335			
Gly	Asp	Pro	Gly	Gln	Pro	Gly	Pro	Pro	Gly	Pro	Ser	Gly	Glu	Ala
1340	1345					1345					1350			
Gly	Pro	Pro	Gly	Pro	Pro	Gly	Lys	Arg	Gly	Pro	Pro	Gly	Ala	Ala
1355	1360					1360					1365			
Gly	Ala	Glu	Gly	Arg	Gln	Gly	Glu	Lys	Gly	Ala	Lys	Gly	Glu	Ala
1370	1375					1375					1380			
Gly	Ala	Glu	Gly	Pro	Pro	Gly	Lys	Thr	Gly	Pro	Val	Gly	Pro	Gln
1385	1390					1390					1395			
Gly	Pro	Ala	Gly	Lys	Pro	Gly	Pro	Glu	Gly	Leu	Arg	Gly	Ile	Pro
1400	1405					1405					1410			
Gly	Pro	Val	Gly	Glu	Gln	Gly	Leu	Pro	Gly	Ala	Ala	Gly	Gln	Asp
1415	1420					1420					1425			
Gly	Pro	Pro	Gly	Pro	Met	Gly	Pro	Pro	Gly	Leu	Pro	Gly	Leu	Lys
1430	1435					1435					1440			
Gly	Asp	Pro	Gly	Ser	Lys	Gly	Glu	Lys	Gly	His	Pro	Gly	Leu	Ile
1445	1450					1450					1455			
Gly	Leu	Ile	Gly	Pro	Pro	Gly	Glu	Gln	Gly	Glu	Lys	Gly	Asp	Arg
1460	1465					1465					1470			
Gly	Leu	Pro	Gly	Thr	Gln	Gly	Ser	Pro	Gly	Ala	Lys	Gly	Asp	Gly
1475	1480					1480					1485			
Gly	Ile	Pro	Gly	Pro	Ala	Gly	Pro	Leu	Gly	Pro	Pro	Gly	Pro	Pro
1490	1495					1495					1500			
Gly	Leu	Pro	Gly	Pro	Gln	Gly	Pro	Lys	Gly	Asn	Lys	Gly	Ser	Thr
1505	1510					1510					1515			
Gly	Pro	Ala	Gly	Gln	Lys	Gly	Asp	Ser	Gly	Leu	Pro	Gly	Pro	Pro
1520	1525					1525					1530			
Gly	Pro	Pro	Gly	Pro	Pro	Gly	Glu	Val	Ile	Gln	Pro	Leu	Pro	Ile
1535	1540					1540					1545			
Leu	Ser	Ser	Lys	Lys	Thr	Arg	Arg	His	Thr	Glu	Gly	Met	Gln	Ala
1550	1555					1555					1560			
Asp	Ala	Asp	Asp	Asn	Ile	Leu	Asp	Tyr	Ser	Asp	Gly	Met	Glu	Glu
1565	1570					1570					1575			
Ile	Phe	Gly	Ser	Leu	Asn	Ser	Leu	Lys	Gln	Asp	Ile	Glu	His	Met
1580	1585													

Cys His Gln Ser Ala Ala Trp Tyr Asp Val Ser Ser Gly Ser Tyr  
 1715 1720 1725  
 Asp Lys Ala Leu Arg Phe Leu Gly Ser Asn Asp Glu Glu Met Ser  
 1730 1735 1740  
 Tyr Asp Asn Asn Pro Phe Ile Lys Thr Leu Tyr Asp Gly Cys Thr  
 1745 1750 1755  
 Ser Arg Lys Gly Tyr Glu Lys Thr Val Ile Glu Ile Asn Thr Pro  
 1760 1765 1770  
 Lys Ile Asp Gln Val Pro Ile Val Asp Val Met Ile Asn Asp Phe  
 1775 1780 1785  
 Gly Asp Gln Asn Gln Lys Phe Gly Phe Glu Val Gly Pro Val Cys  
 1790 1795 1800  
 Phe Leu Gly  
 1805

<210> 209

<211> 669

<212> PRT

<213> Homo sapiens

<400> 209

Met Thr Ala Ala Ala Gly Ser Ala Gly Arg Ala Ala Val Pro Leu Leu  
 1 5 10 15  
 Leu Cys Ala Leu Leu Ala Pro Gly Gly Ala Tyr Val Leu Asp Asp Ser  
 20 25 30  
 Asp Gly Leu Gly Arg Glu Phe Asp Gly Ile Gly Ala Val Ser Gly Gly  
 35 40 45  
 Gly Ala Thr Ser Arg Leu Leu Val Asn Tyr Pro Glu Pro Tyr Arg Ser  
 50 55 60  
 Gln Ile Leu Asp Tyr Leu Phe Lys Pro Asn Phe Gly Ala Ser Leu His  
 65 70 75 80  
 Ile Leu Lys Val Glu Ile Gly Gly Asp Gly Gln Thr Thr Asp Gly Thr  
 85 90 95  
 Glu Pro Ser His Met His Tyr Ala Leu Asp Glu Asn Tyr Phe Arg Gly  
 100 105 110  
 Tyr Glu Trp Trp Leu Met Lys Glu Ala Lys Lys Arg Asn Pro Asn Ile  
 115 120 125  
 Thr Leu Ile Gly Leu Pro Trp Ser Phe Pro Gly Trp Leu Gly Lys Gly  
 130 135 140  
 Phe Asp Trp Pro Tyr Val Asn Leu Gln Leu Thr Ala Tyr Tyr Val Val  
 145 150 155 160  
 Thr Trp Ile Val Gly Ala Lys Arg Tyr His Asp Leu Asp Ile Asp Tyr  
 165 170 175  
 Ile Gly Ile Trp Asn Glu Arg Ser Tyr Asn Ala Asn Tyr Ile Lys Ile  
 180 185 190  
 Leu Arg Lys Met Leu Asn Tyr Gln Gly Leu Gln Arg Val Lys Ile Ile  
 195 200 205  
 Ala Ser Asp Asn Leu Trp Glu Ser Ile Ser Ala Ser Met Leu Leu Asp  
 210 215 220  
 Ala Glu Leu Phe Lys Val Val Asp Val Ile Gly Ala His Tyr Pro Gly  
 225 230 235 240  
 Thr His Ser Ala Lys Asp Ala Lys Leu Thr Gly Lys Lys Leu Trp Ser  
 245 250 255  
 Ser Glu Asp Phe Ser Thr Leu Asn Ser Asp Met Gly Ala Gly Cys Trp  
 260 265 270  
 Gly Arg Ile Leu Asn Gln Asn Tyr Ile Asn Gly Tyr Met Thr Ser Thr  
 275 280 285

Ile Ala Trp Asn Leu Val Ala Ser Tyr Tyr Glu Gln Leu Pro Tyr Gly  
 290 295 300  
 Arg Cys Gly Leu Met Thr Ala Gln Glu Pro Trp Ser Gly His Tyr Val  
 305 310 315 320  
 Val Glu Ser Pro Val Trp Val Ser Ala His Thr Thr Gln Phe Thr Gln  
 325 330 335  
 Pro Gly Trp Tyr Tyr Leu Lys Thr Val Gly His Leu Glu Lys Gly Gly  
 340 345 350  
 Ser Tyr Val Ala Leu Thr Asp Gly Leu Gly Asn Leu Thr Ile Ile Ile  
 355 360 365  
 Glu Thr Met Ser His Lys His Ser Lys Cys Ile Arg Pro Phe Leu Pro  
 370 375 380  
 Tyr Phe Asn Val Ser Gln Gln Phe Ala Thr Phe Val Leu Lys Gly Ser  
 385 390 395 400  
 Phe Ser Glu Ile Pro Glu Leu Gln Val Trp Tyr Thr Lys Leu Gly Lys  
 405 410 415  
 Thr Ser Glu Arg Phe Leu Phe Lys Gln Leu Asp Ser Leu Trp Leu Leu  
 420 425 430  
 Asp Ser Asp Gly Ser Phe Thr Leu Ser Leu His Glu Asp Glu Leu Phe  
 435 440 445  
 Thr Leu Thr Thr Leu Thr Thr Gly Arg Lys Gly Ser Tyr Pro Leu Pro  
 450 455 460  
 Pro Lys Ser Gln Pro Phe Pro Ser Thr Tyr Lys Asp Asp Phe Asn Val  
 465 470 475 480  
 Asp Tyr Pro Phe Phe Ser Glu Ala Pro Asn Phe Ala Asp Gln Thr Gly  
 485 490 495  
 Val Phe Glu Tyr Phe Thr Asn Ile Glu Asp Pro Gly Glu His His Phe  
 500 505 510  
 Thr Leu Arg Gln Val Leu Asn Gln Arg Pro Ile Thr Trp Ala Ala Asp  
 515 520 525  
 Ala Ser Asn Thr Ile Ser Ile Ile Gly Asp Tyr Asn Trp Thr Asn Leu  
 530 535 540  
 Thr Ile Lys Cys Asp Val Tyr Ile Glu Thr Pro Asp Thr Gly Gly Val  
 545 550 555 560  
 Phe Ile Ala Gly Arg Val Asn Lys Gly Gly Ile Leu Ile Arg Ser Ala  
 565 570 575  
 Arg Gly Ile Phe Phe Trp Ile Phe Ala Asn Gly Ser Tyr Arg Val Thr  
 580 585 590  
 Gly Asp Leu Ala Gly Trp Ile Ile Tyr Ala Leu Gly Arg Val Glu Val  
 595 600 605  
 Thr Ala Lys Lys Trp Tyr Thr Leu Thr Leu Thr Ile Lys Gly His Phe  
 610 615 620  
 Ala Ser Gly Met Leu Asn Asp Lys Ser Leu Trp Thr Asp Ile Pro Val  
 625 630 635 640  
 Asn Phe Pro Lys Asn Gly Trp Ala Ala Ile Gly Thr His Ser Phe Glu  
 645 650 655  
 Phe Ala Gln Phe Asp Asn Phe Leu Val Glu Ala Thr Arg  
 660 665

&lt;210&gt; 210

&lt;211&gt; 508

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 210

Met Gln Arg Leu Leu Thr Pro Val Lys Arg Ile Leu Gln Leu Thr Arg  
 1 5 10 15



Ala Val Gln Glu Thr Ser Leu Thr Pro Ala Arg Leu Leu Pro Val Ala  
 20 25 30  
 His Gln Arg Phe Ser Thr Ala Ser Ala Val Pro Leu Ala Lys Thr Asp  
 35 40 45  
 Thr Trp Pro Lys Asp Val Gly Ile Leu Ala Leu Glu Val Tyr Phe Pro  
 50 55 60  
 Ala Gln Tyr Val Asp Gln Thr Asp Leu Glu Lys Tyr Asn Asn Val Glu  
 65 70 75 80  
 Ala Gly Lys Tyr Thr Val Gly Leu Gly Gln Thr Arg Met Gly Phe Cys  
 85 90 95  
 Ser Val Gln Glu Asp Ile Asn Ser Leu Cys Leu Thr Val Val Gln Arg  
 100 105 110  
 Leu Met Glu Arg Ile Gln Leu Pro Trp Asp Ser Val Gly Arg Leu Glu  
 115 120 125  
 Val Gly Thr Glu Thr Ile Ile Asp Lys Ser Lys Ala Val Lys Thr Val  
 130 135 140  
 Leu Met Glu Leu Phe Gln Asp Ser Gly Asn Thr Asp Ile Glu Gly Ile  
 145 150 155 160  
 Asp Thr Thr Asn Ala Cys Tyr Gly Gly Thr Ala Ser Leu Phe Asn Ala  
 165 170 175  
 Ala Asn Trp Met Glu Ser Ser Ser Trp Asp Gly Arg Tyr Ala Met Val  
 180 185 190  
 Val Cys Gly Asp Ile Ala Val Tyr Pro Ser Gly Asn Ala Arg Pro Thr  
 195 200 205  
 Gly Gly Ala Gly Ala Val Ala Met Leu Ile Gly Pro Lys Ala Pro Leu  
 210 215 220  
 Ala Leu Glu Arg Gly Leu Arg Gly Thr His Met Glu Asn Val Tyr Asp  
 225 230 235 240  
 Phe Tyr Lys Pro Asn Leu Ala Ser Glu Tyr Pro Ile Val Asp Gly Lys  
 245 250 255  
 Leu Ser Ile Gln Cys Tyr Leu Arg Ala Leu Asp Arg Cys Tyr Thr Ser  
 260 265 270  
 Tyr Arg Lys Lys Ile Gln Asn Gln Trp Lys Gln Ala Gly Ser Asp Arg  
 275 280 285  
 Pro Phe Thr Leu Asp Asp Leu Gln Tyr Met Ile Phe His Thr Pro Phe  
 290 295 300  
 Cys Lys Met Val Gln Lys Ser Leu Ala Arg Leu Met Phe Asn Asp Phe  
 305 310 315 320  
 Leu Ser Ala Ser Ser Asp Thr Gln Thr Ser Leu Tyr Lys Gly Leu Glu  
 325 330 335  
 Ala Phe Gly Gly Leu Lys Leu Glu Asp Thr Tyr Thr Asn Lys Asp Leu  
 340 345 350  
 Asp Lys Ala Leu Leu Lys Ala Ser Gln Asp Met Phe Asp Lys Lys Thr  
 355 360 365  
 Lys Ala Ser Leu Tyr Leu Ser Thr His Asn Gly Asn Met Tyr Thr Ser  
 370 375 380  
 Ser Leu Tyr Gly Cys Leu Ala Ser Leu Leu Ser His His Ser Ala Gln  
 385 390 395 400  
 Glu Leu Ala Gly Ser Arg Ile Gly Ala Phe Ser Tyr Gly Ser Gly Leu  
 405 410 415  
 Ala Ala Ser Phe Phe Ser Phe Arg Val Ser Gln Asp Ala Ala Pro Gly  
 420 425 430  
 Ser Pro Leu Asp Lys Leu Val Ser Ser Thr Ser Asp Leu Pro Lys Arg  
 435 440 445  
 Leu Ala Ser Arg Lys Cys Val Ser Pro Glu Glu Phe Thr Glu Ile Met  
 450 455 460  
 Asn Gln Arg Glu Gln Phe Tyr His Lys Val Asn Phe Ser Pro Pro Gly  
 465 470 475 480  
 Asp Thr Asn Ser Leu Phe Pro Gly Thr Trp Tyr Leu Glu Arg Val Asp  
 485 490 495  
 Glu Gln His Arg Arg Lys Tyr Ala Arg Arg Pro Val  
 500 505

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&lt;210&gt; 211

&lt;211&gt; 548

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 211

Met	Asn	Ile	Glu	Val	Val	Glu	Val	Leu	Thr	Leu	Asn	Gln	Glu	Val	Ala	
1				5					10					15		
Gly	Pro	Arg	Asn	Ala	Gln	Ile	Gln	Ala	Leu	Tyr	Ala	Glu	Asp	Gly	Ser	
			20					25					30			
Leu	Ser	Ala	Asp	Ala	Pro	Ser	Glu	Gln	Val	Gln	Gln	Gln	Gly	Lys	His	
		35					40					45				
Pro	Gly	Asp	Pro	Glu	Ala	Ala	Arg	Gln	Arg	Phe	Arg	Gln	Phe	Arg	Tyr	
	50					55					60					
Lys	Asp	Met	Thr	Gly	Pro	Arg	Glu	Ala	Leu	Asp	Gln	Leu	Arg	Glu	Leu	
65					70					75					80	
Cys	His	Gln	Trp	Leu	Gln	Pro	Lys	Ala	Arg	Ser	Lys	Glu	Gln	Ile	Leu	
				85					90					95		
Glu	Leu	Leu	Val	Leu	Glu	Gln	Phe	Leu	Gly	Ala	Leu	Pro	Val	Lys	Leu	
			100					105					110			
Arg	Thr	Trp	Val	Glu	Ser	Gln	His	Pro	Glu	Asn	Cys	Gln	Glu	Val	Val	
		115					120					125				
Ala	Leu	Val	Glu	Gly	Val	Thr	Trp	Met	Ser	Glu	Glu	Glu	Val	Leu	Pro	
	130					135					140					
Ala	Gly	Gln	Pro	Ala	Glu	Gly	Thr	Thr	Cys	Cys	Leu	Glu	Val	Thr	Ala	
145					150					155					160	
Gln	Gln	Glu	Glu	Lys	Gln	Glu	Asp	Ala	Ala	Ile	Cys	Pro	Val	Thr	Val	
				165				170						175		
Leu	Pro	Glu	Glu	Pro	Val	Thr	Phe	Gln	Asp	Val	Ala	Val	Asp	Phe	Ser	
			180					185					190			
Arg	Glu	Glu	Trp	Gly	Leu	Leu	Gly	Pro	Thr	Gln	Arg	Thr	Glu	Tyr	Arg	
		195					200					205				
Asp	Val	Met	Leu	Glu	Thr	Phe	Gly	His	Leu	Val	Ser	Val	Gly	Trp	Glu	
	210					215						220				
Thr	Thr	Leu	Glu	Asn	Lys	Glu	Leu	Ala	Pro	Asn	Ser	Asp	Ile	Pro	Glu	
225					230					235					240	
Glu	Glu	Pro	Ala	Pro	Ser	Leu	Lys	Val	Gln	Glu	Ser	Ser	Arg	Asp	Cys	
				245					250					255		
Ala	Leu	Ser	Ser	Thr	Leu	Glu	Asp	Thr	Leu	Gln	Gly	Gly	Val	Gln	Glu	
			260					265					270			
Val	Gln	Asp	Thr	Val	Leu	Lys	Gln	Met	Glu	Ser	Ala	Gln	Glu	Lys	Asp	
		275					280					285				
Leu	Pro	Gln	Lys	Lys	His	Phe	Asp	Asn	Arg	Glu	Ser	Gln	Ala	Asn	Ser	
	290					295					300					
Gly	Ala	Leu	Asp	Thr	Asn	Gln	Val	Ser	Leu	Gln	Lys	Ile	Asp	Asn	Pro	
305					310					315					320	
Glu	Ser	Gln	Ala	Asn	Ser	Gly	Ala	Leu	Asp	Thr	Asn	Gln	Val	Leu	Leu	
				325					330					335		
His	Lys	Ile	Pro	Pro	Arg	Lys	Arg	Leu	Arg	Lys	Arg	Asp	Ser	Gln	Val	
			340					345					350			
Lys	Ser	Met	Lys	His	Asn	Ser	Arg	Val	Lys	Ile	His	Gln	Lys	Ser	Cys	
		355					360					365				
Glu	Arg	Gln	Lys	Ala	Lys	Glu	Gly	Asn	Gly	Cys	Arg	Lys	Thr	Phe	Ser	
	370					375					380					
Arg	Ser	Thr	Lys	Gln	Ile	Thr	Phe	Ile	Arg	Ile	His	Lys	Gly	Ser	Gln	
385					390					395					400	

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Val Cys Arg Cys Ser Glu Cys Gly Lys Ile Phe Arg Asn Pro Arg Tyr  
 405 410 415  
 Phe Ser Val His Lys Lys Ile His Thr Gly Glu Arg Pro Tyr Val Cys  
 420 425 430  
 Gln Asp Cys Gly Lys Gly Phe Val Gln Ser Ser Ser Leu Thr Gln His  
 435 440 445  
 Gln Arg Val His Ser Gly Glu Arg Pro Phe Glu Cys Gln Glu Cys Gly  
 450 455 460  
 Arg Thr Phe Asn Asp Arg Ser Ala Ile Ser Gln His Leu Arg Thr His  
 465 470 475 480  
 Thr Gly Ala Lys Pro Tyr Lys Cys Gln Asp Cys Gly Lys Ala Phe Arg  
 485 490 495  
 Gln Ser Ser His Leu Ile Arg His Gln Arg Thr His Thr Gly Glu Arg  
 500 505 510  
 Pro Tyr Ala Cys Asn Lys Cys Gly Lys Ala Phe Thr Gln Ser Ser His  
 515 520 525  
 Leu Ile Gly His Gln Arg Thr His Asn Arg Thr Lys Arg Lys Lys Lys  
 530 535 540  
 Gln Pro Thr Ser  
 545

&lt;210&gt; 212

&lt;211&gt; 84

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 212

Met Ala Thr Met Glu Asn Lys Val Ile Cys Ala Leu Val Leu Val Ser  
 1 5 10 15  
 Met Leu Ala Leu Gly Thr Leu Ala Glu Ala Gln Thr Glu Thr Cys Thr  
 20 25 30  
 Val Ala Pro Arg Glu Arg Gln Asn Cys Gly Phe Pro Gly Val Thr Pro  
 35 40 45  
 Ser Gln Cys Ala Asn Lys Gly Cys Cys Phe Asp Asp Thr Val Arg Gly  
 50 55 60  
 Val Pro Trp Cys Phe Tyr Pro Asn Thr Ile Asp Val Pro Pro Glu Glu  
 65 70 75 80  
 Glu Cys Glu Phe

&lt;210&gt; 213

&lt;211&gt; 339

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 213

Met Ala Met Gln Met Gln Leu Glu Ala Asn Ala Asp Thr Ser Val Glu  
 1 5 10 15  
 Glu Glu Ser Phe Gly Pro Gln Pro Ile Ser Arg Leu Glu Gln Cys Gly  
 20 25 30  
 Ile Asn Ala Asn Asp Val Lys Lys Leu Glu Glu Ala Gly Phe His Thr  
 35 40 45

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Val Glu Ala Val Ala Tyr Ala Pro Lys Lys Glu Leu Ile Asn Ile Lys  
 50 55 60  
 Gly Ile Ser Glu Ala Lys Ala Asp Lys Ile Leu Ala Glu Ala Ala Lys  
 65 70 75 80  
 Leu Val Pro Met Gly Phe Thr Thr Ala Thr Glu Phe His Gln Arg Arg  
 85 90 95  
 Ser Glu Ile Ile Gln Ile Thr Thr Gly Ser Lys Glu Leu Asp Lys Leu  
 100 105 110  
 Leu Gln Gly Gly Ile Glu Thr Gly Ser Ile Thr Glu Met Phe Gly Glu  
 115 120 125  
 Phe Arg Thr Gly Lys Thr Gln Ile Cys His Thr Leu Ala Val Thr Cys  
 130 135 140  
 Gln Leu Pro Ile Asp Arg Gly Gly Gly Glu Gly Lys Ala Met Tyr Ile  
 145 150 155 160  
 Asp Thr Glu Gly Thr Phe Arg Pro Glu Arg Leu Leu Ala Val Ala Glu  
 165 170 175  
 Arg Tyr Gly Leu Ser Gly Ser Asp Val Leu Asp Asn Val Ala Tyr Ala  
 180 185 190  
 Arg Ala Phe Asn Thr Asp His Gln Thr Gln Leu Leu Tyr Gln Ala Ser  
 195 200 205  
 Ala Met Met Val Glu Ser Arg Tyr Ala Leu Leu Ile Val Asp Ser Ala  
 210 215 220  
 Thr Ala Leu Tyr Arg Thr Asp Tyr Ser Gly Arg Gly Glu Leu Ser Ala  
 225 230 235 240  
 Arg Gln Met His Leu Ala Arg Phe Leu Arg Met Leu Leu Arg Leu Ala  
 245 250 255  
 Asp Glu Phe Gly Val Ala Val Val Ile Thr Asn Gln Val Val Ala Gln  
 260 265 270  
 Val Asp Gly Ala Ala Met Phe Ala Ala Asp Pro Lys Lys Pro Ile Gly  
 275 280 285  
 Gly Asn Ile Ile Ala His Ala Ser Thr Thr Arg Leu Tyr Leu Arg Lys  
 290 295 300  
 Gly Arg Gly Glu Thr Arg Ile Cys Lys Ile Tyr Asp Ser Pro Cys Leu  
 305 310 315 320  
 Pro Glu Ala Glu Ala Met Phe Ala Ile Asn Ala Asp Gly Val Gly Asp  
 325 330 335  
 Ala Lys Asp

&lt;210&gt; 214

&lt;211&gt; 561

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 214

Met Cys Gly Ile Trp Ala Leu Phe Gly Ser Asp Asp Cys Leu Ser Val  
 1 5 10 15  
 Gln Cys Leu Ser Ala Met Lys Ile Ala His Arg Gly Pro Asp Ala Phe  
 20 25 30  
 Arg Phe Glu Asn Val Asn Gly Tyr Thr Asn Cys Cys Phe Gly Phe His  
 35 40 45  
 Arg Leu Ala Val Val Asp Pro Leu Phe Gly Met Gln Pro Ile Arg Val  
 50 55 60  
 Lys Lys Tyr Pro Tyr Leu Trp Leu Cys Tyr Asn Gly Glu Ile Tyr Asn  
 65 70 75 80  
 His Lys Lys Met Gln Gln His Phe Glu Phe Glu Tyr Gln Thr Lys Val  
 85 90 95

Asp Gly Glu Ile Ile Leu His Leu Tyr Asp Lys Gly Gly Ile Glu Gln  
 100 105 110  
 Thr Ile Cys Met Leu Asp Gly Val Phe Ala Phe Val Leu Leu Asp Thr  
 115 120 125  
 Ala Asn Lys Lys Val Phe Leu Gly Arg Asp Thr Tyr Gly Val Arg Pro  
 130 135 140  
 Leu Phe Lys Ala Met Thr Glu Asp Gly Phe Leu Ala Val Cys Ser Glu  
 145 150 155 160  
 Ala Lys Gly Leu Val Thr Leu Lys His Ser Ala Thr Pro Phe Leu Lys  
 165 170 175  
 Val Glu Pro Phe Leu Pro Gly His Tyr Glu Val Leu Asp Leu Lys Pro  
 180 185 190  
 Asn Gly Lys Val Ala Ser Val Glu Met Val Lys Tyr His His Cys Arg  
 195 200 205  
 Asp Glu Pro Leu His Ala Leu Tyr Asp Asn Val Glu Lys Leu Phe Pro  
 210 215 220  
 Gly Phe Glu Ile Glu Thr Val Lys Asn Asn Leu Arg Ile Leu Phe Asn  
 225 230 235 240  
 Asn Ala Val Lys Lys Arg Leu Met Thr Asp Arg Arg Ile Gly Cys Leu  
 245 250 255  
 Leu Ser Gly Gly Leu Asp Ser Ser Leu Val Ala Ala Thr Leu Leu Lys  
 260 265 270  
 Gln Leu Lys Glu Ala Gln Val Gln Tyr Pro Leu Gln Thr Phe Ala Ile  
 275 280 285  
 Gly Met Glu Asp Ser Pro Asp Leu Leu Ala Ala Arg Lys Val Ala Asp  
 290 295 300  
 His Ile Gly Ser Glu His Tyr Glu Val Leu Phe Asn Ser Glu Glu Gly  
 305 310 315 320  
 Ile Gln Ala Leu Asp Glu Val Ile Phe Ser Leu Glu Thr Tyr Asp Ile  
 325 330 335  
 Thr Thr Val Arg Ala Ser Val Gly Met Tyr Leu Ile Ser Lys Tyr Ile  
 340 345 350  
 Arg Lys Asn Thr Asp Ser Val Val Ile Phe Ser Gly Glu Gly Ser Asp  
 355 360 365  
 Glu Leu Thr Gln Gly Tyr Ile Tyr Phe His Lys Ala Pro Ser Pro Glu  
 370 375 380  
 Lys Ala Glu Glu Glu Ser Glu Arg Leu Leu Arg Glu Leu Tyr Leu Phe  
 385 390 395 400  
 Asp Val Leu Arg Ala Asp Arg Thr Thr Ala Ala His Gly Leu Glu Leu  
 405 410 415  
 Arg Val Pro Phe Leu Asp His Arg Phe Ser Ser Tyr Tyr Leu Ser Leu  
 420 425 430  
 Pro Pro Glu Met Arg Ile Pro Lys Asn Gly Ile Glu Lys His Leu Leu  
 435 440 445  
 Arg Glu Thr Phe Glu Asp Ser Asn Leu Ile Pro Lys Glu Ile Leu Trp  
 450 455 460  
 Arg Pro Lys Glu Ala Phe Ser Asp Gly Ile Thr Ser Val Lys Asn Ser  
 465 470 475 480  
 Trp Phe Lys Ile Leu Gln Glu Tyr Val Glu His Gln Val Asp Asp Ala  
 485 490 495  
 Met Met Ala Asn Ala Ala Gln Lys Phe Pro Phe Asn Thr Pro Lys Thr  
 500 505 510  
 Lys Glu Gly Tyr Tyr Tyr Arg Gln Val Phe Glu Arg His Tyr Pro Gly  
 515 520 525  
 Arg Ala Asp Trp Leu Ser His Tyr Trp Met Pro Lys Trp Ile Asn Ala  
 530 535 540  
 Thr Asp Pro Ser Ala Arg Thr Leu Thr His Tyr Lys Ser Ala Val Lys  
 545 550 555 560  
 Ala

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&lt;210&gt; 215

&lt;211&gt; 227

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 215

Met Ala Trp Lys Ser Gly Gly Ala Ser His Ser Glu Leu Ile His Asn  
 1 5 10 15  
 Leu Arg Lys Asn Gly Ile Ile Lys Thr Asp Lys Val Phe Glu Val Met  
 20 25 30  
 Leu Ala Thr Asp Arg Ser His Tyr Ala Lys Cys Asn Pro Tyr Met Asp  
 35 40 45  
 Ser Pro Gln Ser Ile Gly Phe Gln Ala Thr Ile Ser Ala Pro His Met  
 50 55 60  
 His Ala Tyr Ala Leu Glu Leu Leu Phe Asp Gln Leu His Glu Gly Ala  
 65 70 75 80  
 Lys Ala Leu Asp Val Gly Ser Gly Ser Gly Ile Leu Thr Ala Cys Phe  
 85 90 95  
 Ala Arg Met Val Gly Cys Thr Gly Lys Val Ile Gly Ile Asp His Ile  
 100 105 110  
 Lys Glu Leu Val Asp Asp Ser Val Asn Asn Val Arg Lys Asp Asp Pro  
 115 120 125  
 Thr Leu Leu Ser Ser Gly Arg Val Gln Leu Val Val Gly Asp Gly Arg  
 130 135 140  
 Met Gly Tyr Ala Glu Glu Ala Pro Tyr Asp Ala Ile His Val Gly Ala  
 145 150 155 160  
 Ala Ala Pro Val Val Pro Gln Ala Leu Ile Asp Gln Leu Lys Pro Gly  
 165 170 175  
 Gly Arg Leu Ile Leu Pro Val Gly Pro Ala Gly Gly Asn Gln Met Leu  
 180 185 190  
 Glu Gln Tyr Asp Lys Leu Gln Asp Gly Ser Ile Lys Met Lys Pro Leu  
 195 200 205  
 Met Gly Val Ile Tyr Val Pro Leu Thr Asp Lys Glu Lys Gln Trp Ser  
 210 215 220  
 Arg Trp Lys  
 225

&lt;210&gt; 216

&lt;211&gt; 595

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 216

Met Thr Met Thr Leu His Thr Lys Ala Ser Gly Met Ala Leu Leu His  
 1 5 10 15  
 Gln Ile Gln Gly Asn Glu Leu Glu Pro Leu Asn Arg Pro Gln Leu Lys  
 20 25 30  
 Ile Pro Leu Glu Arg Pro Leu Gly Glu Val Tyr Leu Asp Ser Ser Lys  
 35 40 45  
 Pro Ala Val Tyr Asn Tyr Pro Glu Gly Ala Ala Tyr Glu Phe Asn Ala  
 50 55 60

Ala	Ala	Ala	Ala	Asn	Ala	Gln	Val	Tyr	Gly	Gln	Thr	Gly	Leu	Pro	Tyr
65				70						75					80
Gly	Pro	Gly	Ser	Glu	Ala	Ala	Ala	Phe	Gly	Ser	Asn	Gly	Leu	Gly	Gly
			85						90					95	
Phe	Pro	Pro	Leu	Asn	Ser	Val	Ser	Pro	Ser	Pro	Leu	Met	Leu	Leu	His
			100					105					110		
Pro	Pro	Pro	Gln	Leu	Ser	Pro	Phe	Leu	Gln	Pro	His	Gly	Gln	Gln	Val
		115					120					125			
Pro	Tyr	Tyr	Leu	Glu	Asn	Glu	Pro	Ser	Gly	Tyr	Thr	Val	Arg	Glu	Ala
	130					135					140				
Gly	Pro	Pro	Ala	Phe	Tyr	Arg	Pro	Asn	Ser	Asp	Asn	Arg	Arg	Gln	Gly
145				150						155					160
Gly	Arg	Glu	Arg	Leu	Ala	Ser	Thr	Asn	Asp	Lys	Gly	Ser	Met	Ala	Met
			165						170					175	
Glu	Ser	Ala	Lys	Glu	Thr	Arg	Tyr	Cys	Ala	Val	Cys	Asn	Asp	Tyr	Ala
			180					185						190	
Ser	Gly	Tyr	His	Tyr	Gly	Val	Trp	Ser	Cys	Glu	Gly	Cys	Lys	Ala	Phe
		195					200					205			
Phe	Lys	Arg	Ser	Ile	Gln	Gly	His	Asn	Asp	Tyr	Met	Cys	Pro	Ala	Thr
	210					215					220				
Asn	Gln	Cys	Thr	Ile	Asp	Lys	Asn	Arg	Arg	Lys	Ser	Cys	Gln	Ala	Cys
225				230						235					240
Arg	Leu	Arg	Lys	Cys	Tyr	Glu	Val	Gly	Met	Met	Lys	Gly	Gly	Ile	Arg
			245						250					255	
Lys	Asp	Arg	Arg	Gly	Gly	Arg	Met	Leu	Lys	His	Lys	Arg	Gln	Arg	Asp
			260					265					270		
Asp	Gly	Glu	Gly	Arg	Gly	Glu	Val	Gly	Ser	Ala	Gly	Asp	Met	Arg	Ala
		275					280					285			
Ala	Asn	Leu	Trp	Pro	Ser	Pro	Leu	Met	Ile	Lys	Arg	Ser	Lys	Lys	Asn
	290					295					300				
Ser	Leu	Ala	Leu	Ser	Leu	Thr	Ala	Asp	Gln	Met	Val	Ser	Ala	Leu	Leu
305					310					315					320
Asp	Ala	Glu	Pro	Pro	Ile	Leu	Tyr	Ser	Glu	Tyr	Asp	Pro	Thr	Arg	Pro
			325						330					335	
Phe	Ser	Glu	Ala	Ser	Met	Met	Gly	Leu	Leu	Thr	Asn	Leu	Ala	Asp	Arg
			340					345						350	
Glu	Leu	Val	His	Met	Ile	Asn	Trp	Ala	Lys	Arg	Val	Pro	Gly	Phe	Val
		355					360						365		
Asp	Leu	Thr	Leu	His	Asp	Gln	Val	His	Leu	Leu	Glu	Cys	Ala	Trp	Leu
	370					375						380			
Glu	Ile	Leu	Met	Ile	Gly	Leu	Val	Trp	Arg	Ser	Met	Glu	His	Pro	Val
385					390					395					400
Lys	Leu	Leu	Phe	Ala	Pro	Asn	Leu	Leu	Leu	Asp	Arg	Asn	Gln	Gly	Lys
			405						410					415	
Cys	Val	Glu	Gly	Met	Val	Glu	Ile	Phe	Asp	Met	Leu	Leu	Ala	Thr	Ser
			420					425					430		
Ser	Arg	Phe	Arg	Met	Met	Asn	Leu	Gln	Gly	Glu	Glu	Phe	Val	Cys	Leu
		435					440					445			
Lys	Ser	Ile	Ile	Leu	Leu	Asn	Ser	Gly	Val	Tyr	Thr	Phe	Leu	Ser	Ser
		450				455					460				
Thr	Leu	Lys	Ser	Leu	Glu	Lys	Asp	His	Ile	His	Arg	Val	Leu	Asp	
465					470					475				480	
Lys	Ile	Thr	Asp	Thr	Leu	Ile	His	Leu	Met	Ala	Lys	Ala	Gly	Leu	Thr
			485						490					495	
Leu	Gln	Gln	Gln	His	Gln	Arg	Leu	Ala	Gln	Leu	Leu	Leu	Ile	Leu	Ser
			500					505					510		
His	Ile	Arg	His	Met	Ser	Asn	Lys	Gly	Met	Glu	His	Leu	Tyr	Ser	Met
		515					520					525			
Lys	Cys	Lys	Asn	Val	Val	Pro	Leu	Tyr	Asp	Leu	Leu	Leu	Glu	Met	Leu
	530					535						540			
Asp	Ala	His	Arg	Leu	His	Ala	Pro	Thr	Ser	Arg	Gly	Gly	Ala	Ser	Val
545					550					555					560

[illegible]

<400>	217														
Met 1	Ala	Val	Leu	Ala	Ala	Leu	Leu	Arg	Ser	Gly	Ala	Arg	Ser	Arg	Ser
				5					10					15	
Pro	Leu	Leu	Arg	Arg	Leu	Val	Gln	Glu	Ile	Arg	Tyr	Val	Glu	Arg	Ser
			20					25					30		
Tyr	Val	Ser	Lys	Pro	Thr	Leu	Lys	Glu	Val	Val	Ile	Val	Ser	Ala	Thr
		35					40					45			
Arg	Thr	Pro	Ile	Gly	Ser	Phe	Leu	Gly	Ser	Leu	Ser	Leu	Leu	Pro	Ala
	50				55					60					
Thr	Lys	Leu	Gly	Ser	Ile	Ala	Ile	Gln	Gly	Ala	Ile	Glu	Lys	Ala	Gly
65				70					75					80	
Ile	Pro	Lys	Glu	Glu	Val	Lys	Glu	Ala	Tyr	Met	Gly	Asn	Val	Leu	Gln
				85					90				95		
Gly	Gly	Glu	Gly	Gln	Ala	Pro	Thr	Arg	Gln	Ala	Val	Leu	Gly	Ala	Gly
			100					105					110		
Leu	Pro	Ile	Ser	Thr	Pro	Cys	Thr	Thr	Ile	Asn	Lys	Val	Cys	Ala	Ser
		115					120					125			
Gly	Met	Lys	Ala	Ile	Met	Met	Ala	Ser	Gln	Ser	Leu	Met	Cys	Gly	His
	130				135						140				
Gln	Asp	Val	Met	Val	Ala	Gly	Gly	Met	Glu	Ser	Met	Ser	Asn	Val	Pro
145				150					155					160	
Tyr	Val	Met	Asn	Arg	Gly	Ser	Thr	Pro	Tyr	Gly	Gly	Val	Lys	Leu	Glu
			165						170					175	
Asp	Leu	Ile	Val	Lys	Asp	Gly	Leu	Thr	Asp	Val	Tyr	Asn	Lys	Ile	His
			180					185					190		
Met	Gly	Ser	Cys	Ala	Glu	Asn	Thr	Ala	Lys	Lys	Leu	Asn	Ile	Ala	Arg
		195					200					205			
Asn	Glu	Gln	Asp	Ala	Tyr	Ala	Ile	Asn	Ser	Tyr	Thr	Arg	Ser	Lys	Ala
	210					215					220				
Ala	Trp	Glu	Ala	Gly	Lys	Phe	Gly	Asn	Glu	Val	Ile	Pro	Val	Thr	Val
225				230					235					240	
Thr	Val	Lys	Gly	Gln	Pro	Asp	Val	Val	Val	Lys	Glu	Asp	Glu	Glu	Tyr
			245						250					255	
Lys	Arg	Val	Asp	Phe	Ser	Lys	Val	Pro	Lys	Leu	Lys	Thr	Val	Phe	Gln
			260					265					270		
Lys	Glu	Asn	Gly	Thr	Val	Thr	Ala	Ala	Asn	Ala	Ser	Thr	Leu	Asn	Asp
		275					280					285			
Gly	Ala	Ala	Ala	Leu	Val	Leu	Met	Thr	Ala	Asp	Ala	Ala	Lys	Arg	Leu
	290					295					300				
Asn	Val	Thr	Pro	Leu	Ala	Arg	Ile	Val	Ala	Phe	Ala	Asp	Ala	Ala	Val
305				310					315					320	
Glu	Pro	Ile	Asp	Phe	Pro	Ile	Ala	Pro	Val	Tyr	Ala	Ala	Ser	Met	Val
			325						330					335	
Leu	Lys	Asp	Val	Gly	Leu	Lys	Lys	Glu	Asp	Ile	Ala	Met	Trp	Glu	Val
			340					345					350		



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Asn Glu Ala Phe Ser Leu Val Val Leu Ala Asn Ile Lys Met Leu Glu  
 355 360 365  
 Ile Asp Pro Gln Lys Val Asn Ile Asn Gly Gly Ala Val Ser Leu Gly  
 370 375 380  
 His Pro Ile Gly Met Ser Gly Ala Arg Ile Val Gly His Leu Thr His  
 385 390 395 400  
 Ala Leu Lys Gln Gly Glu Tyr Gly Leu Ala Ser Ile Cys Asn Gly Gly  
 405 410 415  
 Gly Gly Ala Ser Ala Met Leu Ile Gln Lys Leu  
 420 425

&lt;210&gt; 218

&lt;211&gt; 273

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 218

Met Ala Ala Ala Asp Gly Ala Leu Pro Glu Ala Ala Ala Leu Glu Gln  
 1 5 10 15  
 Pro Ala Glu Leu Pro Ala Ser Val Arg Ala Ser Ile Glu Arg Lys Arg  
 20 25 30  
 Gln Arg Ala Leu Met Leu Arg Gln Ala Arg Leu Ala Ala Arg Pro Tyr  
 35 40 45  
 Ser Ala Thr Ala Ala Ala Ala Thr Gly Gly Met Ala Asn Val Lys Ala  
 50 55 60  
 Ala Pro Lys Ile Ile Asp Thr Gly Gly Gly Phe Ile Leu Glu Glu Glu  
 65 70 75 80  
 Glu Glu Glu Glu Gln Lys Ile Gly Lys Val Val His Gln Pro Gly Pro  
 85 90 95  
 Val Met Glu Phe Asp Tyr Val Ile Cys Glu Glu Cys Gly Lys Glu Phe  
 100 105 110  
 Met Asp Ser Tyr Leu Met Asn His Phe Asp Leu Pro Thr Cys Asp Asn  
 115 120 125  
 Cys Arg Asp Ala Asp Asp Lys His Lys Leu Ile Thr Lys Thr Glu Ala  
 130 135 140  
 Lys Gln Glu Tyr Leu Leu Lys Asp Cys Asp Leu Glu Lys Arg Glu Pro  
 145 150 155 160  
 Pro Leu Lys Phe Ile Val Lys Lys Asn Pro His His Ser Gln Trp Gly  
 165 170 175  
 Asp Met Lys Leu Tyr Leu Lys Leu Gln Ile Val Lys Arg Ser Leu Glu  
 180 185 190  
 Val Trp Gly Ser Gln Glu Ala Leu Glu Glu Ala Lys Glu Val Arg Gln  
 195 200 205  
 Glu Asn Arg Glu Lys Met Lys Gln Lys Lys Phe Asp Lys Lys Val Lys  
 210 215 220  
 Glu Leu Arg Arg Ala Val Arg Ser Ser Val Trp Lys Arg Glu Thr Ile  
 225 230 235 240  
 Val His Gln His Glu Tyr Gly Pro Glu Glu Asn Leu Glu Asp Asp Met  
 245 250 255  
 Tyr Arg Lys Thr Cys Thr Met Cys Gly His Glu Leu Thr Tyr Glu Lys  
 260 265 270  
 Met

&lt;210&gt; 219

&lt;211&gt; 1227

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 219

Met Asp Ser Phe Asp Leu Ala Leu Leu Gln Glu Trp Asp Leu Glu Ser  
 1 5 10 15  
 Leu Cys Val Tyr Glu Pro Asp Arg Asn Ala Leu Arg Arg Lys Glu Arg  
 20 25 30  
 Glu Arg Arg Asn Gln Glu Thr Gln Asp Asp Gly Thr Phe Asn Ser  
 35 40 45  
 Ser Tyr Ser Leu Phe Ser Glu Pro Tyr Lys Thr Asn Lys Gly Asp Glu  
 50 55 60  
 Leu Ser Asn Arg Ile Gln Asn Thr Leu Gly Asn Tyr Asp Glu Met Lys  
 65 70 75 80  
 Asp Phe Leu Thr Asp Arg Thr Asn Gln Ser His Leu Val Gly Val Pro  
 85 90 95  
 Lys Pro Gly Val Pro Gln Thr Pro Val Asn Lys Ile Asp Glu His Phe  
 100 105 110  
 Val Ala Asp Ser Arg Ala Gln Asn Gln Pro Ser Ser Ile Cys Ser Thr  
 115 120 125  
 Thr Thr Ser Thr Pro Ala Ala Val Pro Val Gln Gln Ser Lys Arg Gly  
 130 135 140  
 Thr Met Gly Trp Gln Lys Ala Gly His Pro Pro Ser Asp Gly Gln Gln  
 145 150 155 160  
 Arg Ala Thr Gln Gln Gly Ser Leu Arg Thr Leu Leu Gly Asp Gly Val  
 165 170 175  
 Gly Arg Gln Gln Pro Arg Ala Lys Gln Val Cys Asn Val Glu Val Gly  
 180 185 190  
 Leu Gln Thr Gln Glu Arg Pro Pro Ala Met Ala Ala Lys His Ser Ser  
 195 200 205  
 Ser Gly His Cys Val Gln Asn Phe Pro Pro Ser Leu Ala Ser Lys Pro  
 210 215 220  
 Ser Leu Val Gln Gln Lys Pro Thr Ala Tyr Val Arg Pro Met Asp Gly  
 225 230 235 240  
 Gln Asp Gln Ala Pro Asp Glu Ser Pro Lys Leu Lys Ser Ser Ser Glu  
 245 250 255  
 Thr Ser Val His Cys Thr Ser Tyr Arg Gly Val Pro Ala Ser Lys Pro  
 260 265 270  
 Glu Pro Ala Arg Ala Lys Ala Lys Leu Ser Lys Phe Ser Ile Pro Lys  
 275 280 285  
 Gln Gly Glu Glu Ser Arg Ser Gly Glu Thr Asn Ser Cys Val Glu Glu  
 290 295 300  
 Ile Ile Arg Glu Met Thr Trp Leu Pro Pro Leu Ser Ala Ile Gln Ala  
 305 310 315 320  
 Pro Gly Lys Val Glu Pro Thr Lys Phe Pro Phe Pro Asn Lys Asp Ser  
 325 330 335  
 Gln Leu Val Ser Ser Gly His Asn Asn Pro Lys Lys Gly Asp Ala Glu  
 340 345 350  
 Pro Glu Ser Pro Asp Asn Gly Thr Ser Asn Thr Ser Met Leu Glu Asp  
 355 360 365  
 Asp Leu Lys Leu Ser Ser Asp Glu Glu Glu Asn Glu Gln Gln Ala Ala  
 370 375 380  
 Gln Arg Thr Ala Leu Arg Ala Leu Ser Asp Ser Ala Val Val Gln Gln  
 385 390 395 400

Pro Asn Cys Arg Thr Ser Val Pro Ser Ser Lys Gly Ser Ser Ser Ser  
 Ser Ser Ser Gly 405 Thr Ser Ser Ser Ser 410 Ser Asp Ser Glu Ser Ser Ser  
 Gly Ser Asp Ser Glu Thr Glu Ser Ser Ser Ser Glu Ser Glu Gly Ser  
 Lys Pro Pro His Phe Ser Ser Pro Glu Ala Glu Pro Ala Ser Ser Asn  
 Lys Trp Gln Leu Asp Lys Trp Leu Asn Lys Val Asn Pro His Lys Pro  
 465 470 475 480  
 Pro Ile Leu Ile Gln Asn Glu Ser His Gly Ser Glu Ser Asn Gln Tyr  
 Tyr Asn Pro Val Lys Glu Asp Val Gln Asp Cys Gly Lys Val Pro Asp  
 Val Cys Gln Pro Ser Leu Arg Glu Lys Glu Ile Lys Ser Thr Cys Lys  
 Glu Glu Gln Arg Pro Arg Thr Ala Asn Lys Ala Pro Gly Ser Lys Gly  
 Val Lys Gln Lys Ser Pro Ala Ala Val Ala Val Ala Val Ser Ala  
 Ala Ala Pro Pro Pro Ala Val Pro Cys Ala Pro Ala Glu Asn Ala Pro  
 Ala Pro Ala Arg Arg Ser Ala Gly Lys Lys Pro Thr Arg Arg Thr Glu  
 Arg Thr Ser Ala Gly Asp Gly Ala Asn Cys His Arg Pro Glu Glu Pro  
 Ala Ala Ala Asp Ala Leu Gly Thr Ser Val Val Val Pro Pro Glu Pro  
 Thr Lys Thr Arg Pro Cys Gly Asn Asn Arg Ala Ser His Arg Lys Glu  
 Leu Arg Ser Ser Val Thr Cys Glu Lys Arg Arg Thr Arg Gly Leu Ser  
 Arg Ile Val Pro Lys Ser Lys Glu Phe Ile Glu Thr Glu Ser Ser Ser  
 Ser Ser Ser Ser Ser Asp Ser Asp Leu Glu Ser Glu Gln Glu Tyr  
 Pro Leu Ser Lys Ala Gln Thr Val Ala Ala Ser Ala Ser Ser Gly Asn  
 Asp Gln Arg Leu Lys Glu Ala Ala Ala Asn Gly Ser Gly Pro Arg  
 Ala Pro Val Gly Ser Ile Asn Ala Arg Thr Thr Ser Asp Ile Ala Lys  
 Glu Leu Glu Glu Gln Phe Tyr Thr Leu Val Pro Phe Gly Arg Asn Glu  
 Leu Leu Ser Pro Leu Lys Asp Ser Asp Glu Ile Arg Ser Leu Trp Val  
 Lys Ile Asp Leu Thr Leu Leu Ser Arg Ile Pro Glu His Leu Pro Gln  
 Glu Pro Gly Val Leu Ser Ala Pro Ala Thr Lys Asp Ser Glu Ser Ala  
 Pro Pro Ser His Thr Ser Asp Thr Pro Ala Glu Lys Ala Leu Pro Lys  
 Ser Lys Arg Lys Arg Lys Cys Asp Asn Glu Asp Asp Tyr Arg Glu Ile  
 Lys Lys Ser Gln Gly Glu Lys Asp Ser Ser Ser Arg Leu Ala Thr Ser  
 Thr Ser Asn Thr Leu Ser Ala Asn His Cys Asn Met Asn Ile Asn Ser  
 Val Ala Ile Pro Ile Asn Lys Asn Glu Lys Met Leu Arg Ser Pro Ile  
 Ser Pro Leu Ser Asp Ala Ser Lys His Lys Tyr Thr Ser Glu Asp Leu  
 885 890 895

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Thr Ser Ser Ser Arg Pro Asn Gly Asn Ser Leu Phe Thr Ser Ala Ser  
 900 905 910  
 Ser Ser Lys Lys Pro Lys Ala Asp Ser Gln Leu Gln Pro His Gly Gly  
 915 920 925  
 Asp Leu Thr Lys Ala Ala His Asn Asn Ser Glu Asn Ile Pro Leu His  
 930 935 940  
 Lys Ser Arg Pro Gln Thr Lys Pro Trp Ser Pro Gly Ser Asn Gly His  
 945 950 955 960  
 Arg Asp Cys Lys Arg Gln Lys Leu Val Phe Asp Asp Met Pro Arg Ser  
 965 970 975  
 Ala Asp Tyr Phe Met Gln Glu Ala Lys Arg Met Lys His Lys Ala Asp  
 980 985 990  
 Ala Met Val Glu Lys Phe Gly Lys Ala Leu Asn Tyr Ala Glu Ala Ala  
 995 1000 1005  
 Leu Ser Phe Ile Glu Cys Gly Asn Ala Met Glu Gln Gly Pro Met  
 1010 1015 1020  
 Glu Ser Lys Ser Pro Tyr Tyr Leu Met Tyr Ser Glu Thr Val Glu  
 1025 1030 1035  
 Leu Ile Arg Tyr Ala Met Arg Leu Lys Thr His Ser Gly Pro Asn  
 1040 1045 1050  
 Ala Thr Pro Glu Asp Lys Gln Leu Ala Ala Leu Cys Tyr Arg Cys  
 1055 1060 1065  
 Leu Ala Leu Leu Tyr Trp Arg Met Phe Arg Leu Lys Arg Asp His  
 1070 1075 1080  
 Ala Val Lys Tyr Ser Lys Ala Leu Ile Asp Tyr Phe Lys Asn Ser  
 1085 1090 1095  
 Ser Lys Ala Ala Gln Ala Pro Ser Pro Trp Gly Ala Ser Gly Lys  
 1100 1105 1110  
 Ser Thr Gly Thr Pro Ser Pro Ile Ser Pro Asn Pro Phe Pro Gly  
 1115 1120 1125  
 Ser Ser Val Gly Ser Gln Gly Ser Leu Ser Asn Ala Ser Ala Leu  
 1130 1135 1140  
 Ser Pro Ser Thr Ile Val Ser Ile Pro Gln Arg Ile His Gln Met  
 1145 1150 1155  
 Ala Ala Asn His Val Ser Ile Thr Asn Ser Ile Leu His Ser Tyr  
 1160 1165 1170  
 Asp Tyr Trp Glu Met Ala Asp Asn Leu Ala Lys Glu Asn Arg Glu  
 1175 1180 1185  
 Phe Phe Asn Asp Leu Asp Leu Leu Met Gly Pro Val Thr Leu His  
 1190 1195 1200  
 Ser Ser Met Glu His Leu Val Gln Tyr Ser Gln Gln Gly Leu His  
 1205 1210 1215  
 Trp Leu Arg Asn Ser Ala His Leu Ser  
 1220 1225

&lt;210&gt; 220

&lt;211&gt; 680

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 220

Met Leu Pro Gln Ile Pro Phe Leu Leu Leu Val Ser Leu Asn Leu Val  
 1 5 10 15  
 His Gly Val Phe Tyr Ala Glu Arg Tyr Gln Met Pro Thr Gly Ile Lys  
 20 25 30  
 Gly Pro Leu Pro Asn Thr Lys Thr Gln Phe Phe Ile Pro Tyr Thr Ile  
 35 40 45

Lys Ser Lys Gly Ile Ala Val Arg Gly Glu Gln Gly Thr Pro Gly Pro  
 50 55 60  
 Pro Gly Pro Ala Gly Pro Arg Gly His Pro Gly Pro Ser Gly Pro Pro  
 65 70 75 80  
 Gly Lys Pro Gly Tyr Gly Ser Pro Gly Leu Gln Gly Glu Pro Gly Leu  
 85 90 95  
 Pro Gly Pro Pro Gly Pro Ser Ala Val Gly Lys Pro Gly Val Pro Gly  
 100 105 110  
 Leu Pro Gly Lys Pro Gly Glu Arg Gly Pro Tyr Gly Pro Lys Gly Asp  
 115 120 125  
 Val Gly Pro Ala Gly Leu Pro Gly Pro Arg Gly Pro Gly Pro Pro  
 130 135 140  
 Gly Ile Pro Gly Pro Ala Gly Ile Ser Val Pro Gly Lys Pro Gly Gln  
 145 150 155 160  
 Gln Gly Pro Thr Gly Ala Pro Gly Pro Arg Gly Phe Pro Gly Glu Lys  
 165 170 175  
 Gly Ala Pro Gly Val Pro Gly Met Asn Gly Gln Lys Gly Glu Met Gly  
 180 185 190  
 Tyr Gly Ala Pro Gly Arg Pro Gly Glu Arg Gly Leu Pro Gly Pro Gln  
 195 200 205  
 Gly Pro Thr Gly Pro Ser Gly Pro Pro Gly Val Gly Lys Arg Gly Glu  
 210 215 220  
 Asn Gly Val Pro Gly Gln Pro Gly Ile Lys Gly Asp Arg Gly Phe Pro  
 225 230 235 240  
 Gly Glu Met Gly Pro Ile Gly Pro Pro Gly Pro Gln Gly Pro Pro Gly  
 245 250 255  
 Glu Arg Gly Pro Glu Gly Ile Gly Lys Pro Gly Ala Ala Gly Ala Pro  
 260 265 270  
 Gly Gln Pro Gly Ile Pro Gly Thr Lys Gly Leu Pro Gly Ala Pro Gly  
 275 280 285  
 Ile Ala Gly Pro Pro Gly Pro Gly Phe Gly Lys Pro Gly Leu Pro  
 290 295 300  
 Gly Leu Lys Gly Glu Arg Gly Pro Ala Gly Leu Pro Gly Gly Pro Gly  
 305 310 315 320  
 Ala Lys Gly Glu Gln Gly Pro Ala Gly Leu Pro Gly Lys Pro Gly Leu  
 325 330 335  
 Thr Gly Pro Pro Gly Asn Met Gly Pro Gln Gly Pro Lys Gly Ile Pro  
 340 345 350  
 Gly Ser His Gly Leu Pro Gly Pro Lys Gly Glu Thr Gly Pro Ala Gly  
 355 360 365  
 Pro Ala Gly Tyr Pro Gly Ala Lys Gly Glu Arg Gly Ser Pro Gly Ser  
 370 375 380  
 Asp Gly Lys Pro Gly Tyr Pro Gly Lys Pro Gly Leu Asp Gly Pro Lys  
 385 390 395 400  
 Gly Asn Pro Gly Leu Pro Gly Pro Lys Gly Asp Pro Gly Val Gly Gly  
 405 410 415  
 Pro Pro Gly Leu Pro Gly Pro Val Gly Pro Ala Gly Ala Lys Gly Met  
 420 425 430  
 Pro Gly His Asn Gly Glu Ala Gly Pro Arg Gly Ala Pro Gly Ile Pro  
 435 440 445  
 Gly Thr Arg Gly Pro Ile Gly Pro Pro Gly Ile Pro Gly Phe Pro Gly  
 450 455 460  
 Ser Lys Gly Asp Pro Gly Ser Pro Gly Pro Pro Gly Pro Ala Gly Ile  
 465 470 475 480  
 Ala Thr Lys Gly Leu Asn Gly Pro Thr Gly Pro Pro Gly Pro Pro Gly  
 485 490 495  
 Pro Arg Gly His Ser Gly Glu Pro Gly Leu Pro Gly Pro Pro Gly Pro  
 500 505 510  
 Pro Gly Pro Pro Gly Gln Ala Val Met Pro Glu Gly Phe Ile Lys Ala  
 515 520 525  
 Gly Gln Arg Pro Ser Leu Ser Gly Thr Pro Leu Val Ser Ala Asn Gln  
 530 535 540

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Gly Val Thr Gly Met Pro Val Ser Ala Phe Thr Val Ile Leu Ser Lys  
 545 550 555 560  
 Ala Tyr Pro Ala Ile Gly Thr Pro Ile Pro Phe Asp Lys Ile Leu Tyr  
 565 570 575  
 Asn Arg Gln Gln His Tyr Asp Pro Arg Thr Gly Ile Phe Thr Cys Gln  
 580 585 590  
 Ile Pro Gly Ile Tyr Tyr Phe Ser Tyr His Val His Val Lys Gly Thr  
 595 600 605  
 His Val Trp Val Gly Leu Tyr Lys Asn Gly Thr Pro Val Met Tyr Thr  
 610 615 620  
 Tyr Asp Glu Tyr Thr Lys Gly Tyr Leu Asp Gln Ala Ser Gly Ser Ala  
 625 630 635 640  
 Ile Ile Asp Leu Thr Glu Asn Asp Gln Val Trp Leu Gln Leu Pro Asn  
 645 650 655  
 Ala Glu Ser Asn Gly Leu Tyr Ser Ser Glu Tyr Val His Ser Ser Phe  
 660 665 670  
 Ser Gly Phe Leu Val Ala Pro Met  
 675 680

&lt;210&gt; 221

&lt;211&gt; 622

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 221  
 Met Gly Leu Tyr Gly Gln Ala Cys Pro Ser Val Thr Ser Leu Arg Met  
 1 5 10 15  
 Thr Ser Glu Leu Glu Ser Ser Leu Thr Ser Met Asp Trp Leu Pro Gln  
 20 25 30  
 Leu Thr Met Arg Ala Ala Ile Gln Lys Ser Asp Ala Thr Gln Asn Ala  
 35 40 45  
 His Gly Thr Gly Ile Ser Lys Lys Asn Ala Leu Leu Asp Pro Asn Thr  
 50 55 60  
 Thr Leu Asp Gln Glu Glu Val Gln Gln His Lys Asp Gly Lys Pro Pro  
 65 70 75 80  
 Tyr Ser Tyr Ala Ser Leu Ile Thr Phe Ala Ile Asn Ser Ser Pro Lys  
 85 90 95  
 Lys Lys Met Thr Leu Ser Glu Ile Tyr Gln Trp Ile Cys Asp Asn Phe  
 100 105 110  
 Pro Tyr Tyr Arg Glu Ala Gly Ser Gly Trp Lys Asn Ser Ile Arg His  
 115 120 125  
 Asn Leu Ser Leu Asn Lys Cys Phe Leu Lys Val Pro Arg Ser Lys Asp  
 130 135 140  
 Asp Pro Gly Lys Gly Ser Tyr Trp Ala Ile Asp Thr Asn Pro Lys Glu  
 145 150 155 160  
 Asp Ala Leu Pro Thr Arg Pro Lys Lys Arg Ala Arg Ser Val Glu Arg  
 165 170 175  
 Ala Ser Thr Pro Tyr Ser Ile Asp Ser Asp Ser Leu Gly Met Glu Cys  
 180 185 190  
 Ile Ile Ser Gly Ser Ala Ser Pro Thr Leu Ala Ile Asn Thr Val Thr  
 195 200 205  
 Asn Lys Val Thr Leu Tyr Asn Thr Asp Gln Asp Gly Ser Asp Ser Pro  
 210 215 220  
 Arg Ser Ser Leu Asn Asn Ser Leu Ser Asp Gln Ser Leu Ala Ser Val  
 225 230 235 240  
 Asn Leu Asn Ser Val Gly Ser Val His Ser Tyr Thr Pro Val Thr Ser  
 245 250 255

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His Pro Glu Ser Val Ser Gln Ser Leu Thr Pro Gln Gln Gln Pro Gln  
 Tyr Asn Leu 260 Pro Glu Arg Asp Lys 265 Gln Leu Leu Phe Ser 270 Glu Tyr Asn  
 Phe Glu Asp 275 Leu Ser Ala Ser 280 Phe Arg Ser Leu Tyr 285 Lys Ser Val Phe  
 Glu Gln Ser Leu Ser 290 295 Gln Gln Gly Leu Met Asn Ile Pro Ser Glu Ser  
 Ser Gln Gln Ser His 305 310 Thr Ser Cys Thr Tyr Gln His Ser Pro Ser Ser  
 Thr Val Ser Thr His 325 330 Asn Gln Ser Ser Leu Ser Asn Ser  
 His Gly Ser Gly Leu Asn Thr 340 345 Thr Gly Ser Asn Ser Val Ala Gln Val  
 Ser Leu Ser His Pro Gln Met 355 360 His Pro Gln Pro Ser 365 Pro His Pro Pro  
 His Arg Pro His Gly Leu Pro 370 375 Gln His Pro Gln Arg Ser Pro His Pro  
 Ala Pro His Pro Gln Gln His Ser Gln Leu Gln Ser Pro His Pro Gln  
 His Pro Ser Pro 385 390 His Gln His Ile Gln His His Pro Asn His Gln His  
 Gln Thr Leu Thr His Gln Ala Pro 405 410 Pro Pro Pro Gln Gln Val Ser Cys  
 Asn Ser Gly Val Ser Asn Asp 420 425 Trp Tyr Ala Thr Leu Asp Met Leu Lys  
 Glu Ser Cys Arg Ile Ala Ser 435 440 Ser Val Asn Trp Ser Asp Val Asp Leu  
 Ser Gln Phe Gln Gly Leu Met Glu Ser Met Arg Gln Ala Asp Leu Lys  
 Asn Trp Ser Leu Asp Gln Val Gln Phe Ala Asp Leu Cys Ser Ser Leu  
 Asn Gln Phe Phe Thr Gln Thr Gly 450 455 Leu Ile His Ser Gln Ser Asn Val  
 Gln Gln Asn Val Cys His Gly 465 470 Ala Met His Pro Thr Lys Pro Ser Gln  
 His Ile Gly Thr Gly Asn Leu Tyr Ile Asp Ser Arg Gln Asn Leu Pro  
 Pro Ser Val Met Pro Pro Pro Gly Tyr Pro 480 485 His Ile Pro Gln Ala Leu  
 Ser Thr Pro Gly Thr Thr Met Ala Gly His His Arg Ala Met Asn Gln  
 Gln His Met 490 495 Pro Ser Gln Ala Phe Gln Met Arg Arg Ser Leu Pro  
 Pro Asp Asp Ile Gln Asp Asp 500 505 Phe Asp Trp Asp Ser Ile Val  
 610 615 620

&lt;210&gt; 222

&lt;211&gt; 441

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 222

Met Val Pro Pro Lys Leu His Val Leu Phe Cys Leu Cys Gly Cys Leu  
 1 5 10 15  
 Ala Val Val Tyr Pro Phe Asp Trp Gln Tyr Ile Asn Pro Val Ala His  
 20 25 30

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Met Lys Ser Ser Ala Trp Val Asn Lys Ile Gln Val Leu Met Ala Ala  
 35 40 45  
 Ala Ser Phe Gly Gln Thr Lys Ile Pro Arg Gly Asn Gly Pro Tyr Ser  
 50 55 60  
 Val Gly Cys Thr Asp Leu Met Phe Asp His Thr Asn Lys Gly Thr Phe  
 65 70 75 80  
 Leu Arg Leu Tyr Tyr Pro Ser Gln Asp Asn Asp Arg Leu Asp Thr Leu  
 85 90 95  
 Trp Ile Pro Asn Lys Glu Tyr Phe Trp Gly Leu Ser Lys Phe Leu Gly  
 100 105 110  
 Thr His Trp Leu Met Gly Asn Ile Leu Arg Leu Leu Phe Gly Ser Met  
 115 120 125  
 Thr Thr Pro Ala Asn Trp Asn Ser Pro Leu Arg Pro Gly Glu Lys Tyr  
 130 135 140  
 Pro Leu Val Val Phe Ser His Gly Leu Gly Ala Phe Arg Thr Leu Tyr  
 145 150 155 160  
 Ser Ala Ile Gly Ile Asp Leu Ala Ser His Gly Phe Ile Val Ala Ala  
 165 170 175  
 Val Glu His Arg Asp Arg Ser Ala Ser Ala Thr Tyr Tyr Phe Lys Asp  
 180 185 190  
 Gln Ser Ala Ala Glu Ile Gly Asp Lys Ser Trp Leu Tyr Leu Arg Thr  
 195 200 205  
 Leu Lys Gln Glu Glu Glu Thr His Ile Arg Asn Glu Gln Val Arg Gln  
 210 215 220  
 Arg Ala Lys Glu Cys Ser Gln Ala Leu Ser Leu Ile Leu Asp Ile Asp  
 225 230 235 240  
 His Gly Lys Pro Val Lys Asn Ala Leu Asp Leu Lys Phe Asp Met Glu  
 245 250 255  
 Gln Leu Lys Asp Ser Ile Asp Arg Glu Lys Ile Ala Val Ile Gly His  
 260 265 270  
 Ser Phe Gly Gly Ala Thr Val Ile Gln Thr Leu Ser Glu Asp Gln Arg  
 275 280 285  
 Phe Arg Cys Gly Ile Ala Leu Asp Ala Trp Met Phe Pro Leu Gly Asp  
 290 295 300  
 Glu Val Tyr Ser Arg Ile Pro Gln Pro Leu Phe Phe Ile Asn Ser Glu  
 305 310 315 320  
 Tyr Phe Gln Tyr Pro Ala Asn Ile Ile Lys Met Lys Lys Cys Tyr Ser  
 325 330 335  
 Pro Asp Lys Glu Arg Lys Met Ile Thr Ile Arg Gly Ser Val His Gln  
 340 345 350  
 Asn Phe Ala Asp Phe Thr Phe Ala Thr Gly Lys Ile Ile Gly His Met  
 355 360 365  
 Leu Lys Leu Lys Gly Asp Ile Asp Ser Asn Ala Ala Ile Asp Leu Ser  
 370 375 380  
 Asn Lys Ala Ser Leu Ala Phe Leu Gln Lys His Leu Gly Leu His Lys  
 385 390 395 400  
 Asp Phe Asp Gln Trp Asp Cys Leu Ile Glu Gly Asp Asp Glu Asn Leu  
 405 410 415  
 Ile Pro Gly Thr Asn Ile Asn Thr Thr Asn Gln His Ile Met Leu Gln  
 420 425 430  
 Asn Ser Ser Gly Ile Glu Lys Tyr Asn  
 435 440

&lt;210&gt; 223

&lt;211&gt; 148

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens



&lt;400&gt; 223

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Met Arg Gly Arg Glu Leu Pro Leu Val Leu Leu Ala Leu Val Leu Cys
1          5          10          15
Leu Ala Pro Arg Gly Arg Ala Val Pro Leu Pro Ala Gly Gly Gly Thr
          20          25          30
Val Leu Thr Lys Met Tyr Pro Arg Gly Asn His Trp Ala Val Gly His
          35          40          45
Leu Met Gly Lys Lys Ser Thr Gly Glu Ser Ser Ser Val Ser Glu Arg
          50          55          60
Gly Ser Leu Lys Gln Gln Leu Arg Glu Tyr Ile Arg Trp Glu Glu Ala
          65          70          75          80
Ala Arg Asn Leu Leu Gly Leu Ile Glu Ala Lys Glu Asn Arg Asn His
          85          90          95
Gln Pro Pro Gln Pro Lys Ala Leu Gly Asn Gln Gln Pro Ser Trp Asp
          100          105          110
Ser Glu Asp Ser Ser Asn Phe Lys Asp Val Gly Ser Lys Gly Lys Val
          115          120          125
Gly Arg Leu Ser Ala Pro Gly Ser Gln Arg Glu Gly Arg Asn Pro Gln
          130          135          140
Leu Asn Gln Gln
145

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&lt;210&gt; 224

&lt;211&gt; 491

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 224

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Met Glu Leu Ser Val Leu Leu Phe Leu Ala Leu Leu Thr Gly Leu Leu
1          5          10          15
Leu Leu Leu Val Gln Arg His Pro Asn Thr His Asp Arg Leu Pro Pro
          20          25          30
Gly Pro Arg Pro Leu Pro Leu Leu Gly Asn Leu Leu Gln Met Asp Arg
          35          40          45
Arg Gly Leu Leu Lys Ser Phe Leu Arg Phe Arg Glu Lys Tyr Gly Asp
          50          55          60
Val Phe Thr Val His Leu Gly Pro Arg Pro Val Val Met Leu Cys Gly
          65          70          75          80
Val Glu Ala Ile Arg Glu Ala Leu Val Asp Lys Ala Glu Ala Phe Ser
          85          90          95
Gly Arg Gly Lys Ile Ala Met Val Asp Pro Phe Phe Arg Gly Tyr Gly
          100          105          110
Val Ile Phe Ala Asn Gly Asn Arg Trp Lys Val Leu Arg Arg Phe Ser
          115          120          125
Val Thr Thr Met Arg Asp Phe Gly Met Gly Lys Arg Ser Val Glu Glu
          130          135          140
Arg ile Gln Glu Glu Ala Gln Cys Leu Ile Glu Glu Leu Arg Lys Ser
          145          150          155          160
Lys Gly Ala Leu Met Asp Pro Thr Phe Leu Phe Gln Ser Ile Thr Ala
          165          170          175
Asn ile ile Cys Ser ile Val Phe Gly Lys Arg Phe His Tyr Gln Asp
          180          185          190
Gln Glu Phe Leu Lys Met Leu Asn Leu Phe Tyr Gln Thr Phe Ser Leu
          195          200          205
Ile Ser Ser Val Phe Gly Gln Leu Phe Glu Leu Phe Ser Gly Phe Leu
          210          215          220

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Lys Tyr Phe Pro Gly Ala His Arg Gln Val Tyr Lys Asn Leu Gln Glu  
 225 230 235 240  
 Ile Asn Ala Tyr Ile Gly His Ser Val Glu Lys His Arg Glu Thr Leu  
 245 250 255  
 Asp Pro Ser Ala Pro Lys Asp Leu Ile Asp Thr Tyr Leu Leu His Met  
 260 265 270  
 Glu Lys Glu Lys Ser Asn Ala His Ser Glu Phe Ser His Gln Asn Leu  
 275 280 285  
 Asn Leu Asn Thr Leu Ser Leu Phe Phe Ala Gly Thr Glu Thr Thr Ser  
 290 295 300  
 Thr Thr Leu Arg Tyr Gly Phe Leu Leu Met Leu Lys Tyr Pro His Val  
 305 310 315 320  
 Ala Glu Arg Val Tyr Arg Glu Ile Glu Gln Val Ile Gly Pro His Arg  
 325 330 335  
 Pro Pro Glu Leu His Asp Arg Ala Lys Met Pro Tyr Thr Glu Ala Val  
 340 345 350  
 Ile Tyr Glu Ile Gln Arg Phe Ser Asp Leu Leu Pro Met Gly Val Pro  
 355 360 365  
 His Ile Val Thr Gln His Thr Ser Phe Arg Gly Tyr Ile Ile Pro Lys  
 370 375 380  
 Asp Thr Glu Val Phe Leu Ile Leu Ser Thr Ala Leu His Asp Pro His  
 385 390 395 400  
 Tyr Phe Glu Lys Pro Asp Ala Phe Asn Pro Asp His Phe Leu Asp Ala  
 405 410 415  
 Asn Gly Ala Leu Lys Lys Thr Glu Ala Phe Ile Pro Phe Ser Leu Gly  
 420 425 430  
 Lys Arg Ile Cys Leu Gly Glu Gly Ile Ala Arg Ala Glu Leu Phe Leu  
 435 440 445  
 Phe Phe Thr Thr Ile Leu Gln Asn Phe Ser Met Ala Ser Pro Val Ala  
 450 455 460  
 Pro Glu Asp Ile Asp Leu Thr Pro Gln Glu Cys Gly Val Gly Lys Ile  
 465 470 475 480  
 Pro Pro Thr Tyr Gln Ile Arg Phe Leu Pro Arg  
 485 490

&lt;210&gt; 225

&lt;211&gt; 359

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 225

Met Val Arg Pro Met Leu Leu Leu Ser Leu Gly Leu Leu Ala Gly Leu  
 1 5 10 15  
 Leu Pro Ala Leu Ala Ala Cys Pro Gln Asn Cys His Cys His Ser Asp  
 20 25 30  
 Leu Gln His Val Ile Cys Asp Lys Val Gly Leu Gln Lys Ile Pro Lys  
 35 40 45  
 Val Ser Glu Lys Thr Lys Leu Leu Asn Leu Gln Arg Asn Asn Phe Pro  
 50 55 60  
 Val Leu Ala Ala Asn Ser Phe Arg Ala Met Pro Asn Leu Val Ser Leu  
 65 70 75 80  
 His Leu Gln His Cys Gln Ile Arg Glu Val Ala Ala Gly Ala Phe Arg  
 85 90 95  
 Gly Leu Lys Gln Leu Ile Tyr Leu Tyr Leu Ser His Asn Asp Ile Arg  
 100 105 110  
 Val Val Arg Ala Gly Ala Phe Asp Leu Thr Glu Leu Thr Tyr Leu  
 115 120 125

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Tyr Leu Asp His Asn Lys Val Thr Glu Leu Pro Arg Gly Leu Leu Ser  
 130 135 140  
 Pro Leu Val Asn Leu Phe Ile Leu Gln Leu Asn Asn Asn Lys Ile Arg  
 145 150 155 160  
 Glu Leu Arg Ala Gly Pro Phe Gln Gly Ala Lys Asp Leu Arg Trp Leu  
 165 170 175  
 Tyr Leu Ser Glu Asn Ala Leu Ser Ser Leu Gln Pro Gly Ala Leu Asp  
 180 185 190  
 Asp Val Glu Asn Leu Ala Lys Phe His Val Asp Arg Asn Gln Leu Ser  
 195 200 205  
 Ser Tyr Pro Ser Ala Ala Leu Ser Lys Leu Arg Val Val Glu Glu Leu  
 210 215 220  
 Lys Leu Ser His Asn Pro Leu Lys Ser Ile Pro Asp Asn Ala Phe Gln  
 225 230 235 240  
 Ser Phe Gly Arg Tyr Leu Glu Thr Leu Trp Leu Asp Asn Thr Asn Leu  
 245 250 255  
 Glu Lys Phe Ser Asp Gly Ala Phe Leu Gly Val Thr Thr Leu Lys His  
 260 265 270  
 Val His Leu Glu Asn Asn Arg Leu Asn Gln Leu Pro Ser Asn Phe Pro  
 275 280 285  
 Phe Asp Ser Leu Glu Thr Leu Ala Leu Thr Asn Asn Pro Trp Lys Cys  
 290 295 300  
 Thr Cys Gln Leu Arg Gly Leu Arg Arg Trp Leu Glu Ala Lys Ala Ser  
 305 310 315 320  
 Arg Pro Asp Ala Thr Cys Ala Ser Pro Ala Lys Phe Lys Gly Gln His  
 325 330 335  
 Ile Arg Asp Thr Asp Ala Phe Arg Ser Cys Lys Phe Pro Thr Lys Arg  
 340 345 350  
 Ser Lys Lys Ala Gly Arg His  
 355

&lt;210&gt; 226

&lt;211&gt; 276

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 226

Met Leu Ala Trp Arg Asp Gly Glu Leu Glu Ala Glu Thr Ser Ser Ser  
 1 5 10 15  
 Leu Phe Leu Leu Ala Met Gln Val Trp Met Cys Gly Gly Arg Met Glu  
 20 25 30  
 Asp Ile Pro Cys Ser Arg Val Gly His Ile Tyr Arg Lys Tyr Val Pro  
 35 40 45  
 Tyr Lys Val Pro Ala Gly Val Ser Leu Ala Arg Val Arg Thr Leu Lys  
 50 55 60  
 Arg Val Ala Glu Val Trp Met Asp Glu Tyr Ala Glu Tyr Ile Tyr Gln  
 65 70 75 80  
 Arg Arg Pro Glu Tyr Arg His Leu Ser Ala Gly Asp Val Ala Val Gln  
 85 90 95  
 Lys Lys Leu Arg Ser Ser Leu Asn Cys Lys Ser Phe Lys Trp Phe Met  
 100 105 110  
 Thr Lys Ile Ala Trp Asp Leu Pro Lys Phe Tyr Pro Pro Val Glu Pro  
 115 120 125  
 Pro Ala Ala Ala Trp Gly Glu Ile Arg Asn Val Gly Thr Gly Leu Cys  
 130 135 140  
 Ala Asp Thr Lys His Gly Ala Leu Gly Ser Pro Leu Arg Leu Glu Gly  
 145 150 155 160

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Cys Val Arg Gly Arg Gly Glu Ala Ala Trp Asn Asn Met Gln Val Phe  
 165 170 175  
 Thr Phe Thr Trp Arg Glu Asp Ile Arg Pro Gly Asp Pro Gln His Thr  
 180 185 190  
 Lys Lys Phe Cys Phe Asp Ala Ile Ser His Thr Ser Pro Val Thr Leu  
 195 200 205  
 Tyr Asp Cys His Ser Met Lys Gly Asn Gln Leu Trp Lys Tyr Arg Lys  
 210 215 220  
 Asp Lys Thr Leu Tyr His Pro Val Ser Gly Ser Cys Met Asp Cys Ser  
 225 230 235 240  
 Glu Ser Asp His Arg Ile Phe Met Asn Thr Cys Asn Pro Ser Ser Leu  
 245 250 255  
 Thr Gln Gln Trp Leu Phe Glu His Thr Asn Ser Thr Val Leu Glu Lys  
 260 265 270  
 Phe Asn Arg Asn  
 275

&lt;210&gt; 227

&lt;211&gt; 161

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 227

Met Thr Leu Glu Glu Leu Val Ala Cys Asp Asn Ala Ala Gln Lys Met  
 1 5 10 15  
 Gln Thr Val Thr Ala Ala Val Glu Glu Leu Leu Val Ala Ala Gln Arg  
 20 25 30  
 Gln Asp Arg Leu Thr Val Gly Val Tyr Glu Ser Ala Lys Leu Met Asn  
 35 40 45  
 Val Asp Pro Asp Ser Val Val Leu Cys Leu Leu Ala Ile Asp Glu Glu  
 50 55 60  
 Glu Glu Asp Asp Ile Ala Leu Gln Ile His Phe Thr Leu Ile Gln Ser  
 65 70 75 80  
 Phe Cys Cys Asp Asn Asp Ile Asn Ile Val Arg Val Ser Gly Asn Ala  
 85 90 95  
 Arg Leu Ala Gln Leu Leu Gly Glu Pro Ala Glu Thr Gln Gly Thr Thr  
 100 105 110  
 Glu Ala Arg Asp Leu His Cys Leu Pro Phe Leu Gln Asn Pro His Thr  
 115 120 125  
 Asp Ala Trp Lys Ser His Gly Leu Val Glu Val Ala Ser Tyr Cys Glu  
 130 135 140  
 Glu Ser Arg Gly Asn Asn Gln Trp Val Pro Tyr Ile Ser Leu Gln Glu  
 145 150 155 160  
 Arg

&lt;210&gt; 228

&lt;211&gt; 281

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 228  
 Met Ala Ser Arg Gly Arg Arg Pro Glu His Gly Gly Pro Pro Glu Leu  
 1 5 10 15  
 Phe Tyr Asp Glu Thr Glu Ala Arg Lys Tyr Val Arg Asn Ser Arg Met  
 20 25 30  
 Ile Asp Ile Gln Thr Arg Met Ala Gly Arg Ala Leu Glu Leu Tyr  
 35 40 45  
 Leu Pro Glu Asn Lys Pro Cys Tyr Leu Leu Asp Ile Gly Cys Gly Thr  
 50 55 60  
 Gly Leu Ser Gly Ser Tyr Leu Ser Asp Glu Gly His Tyr Trp Val Gly  
 65 70 75 80  
 Leu Asp Ile Ser Pro Ala Met Leu Asp Glu Ala Val Asp Arg Glu Ile  
 85 90 95  
 Glu Gly Asp Leu Leu Gly Asp Met Gly Gln Gly Ile Pro Phe Lys  
 100 105 110  
 Pro Gly Thr Phe Asp Gly Cys Ile Ser Ile Ser Ala Val Gln Trp Leu  
 115 120 125  
 Cys Asn Ala Asn Lys Lys Ser Glu Asn Pro Ala Lys Arg Leu Tyr Cys  
 130 135 140  
 Phe Phe Ala Ser Leu Phe Ser Val Leu Val Arg Gly Ser Arg Ala Val  
 145 150 155 160  
 Leu Gln Leu Tyr Pro Glu Asn Ser Glu Gln Leu Glu Leu Ile Thr Thr  
 165 170 175  
 Gln Ala Thr Lys Ala Gly Phe Ser Gly Gly Met Val Val Asp Tyr Pro  
 180 185 190  
 Asn Ser Ala Lys Ala Lys Lys Phe Tyr Leu Cys Leu Phe Ser Gly Pro  
 195 200 205  
 Ser Thr Phe Ile Pro Glu Gly Leu Ser Glu Asn Gln Asp Glu Val Glu  
 210 215 220  
 Pro Arg Glu Ser Val Phe Thr Asn Glu Arg Phe Pro Leu Arg Met Ser  
 225 230 235 240  
 Arg Arg Gly Met Val Arg Lys Ser Arg Ala Trp Val Leu Glu Lys Lys  
 245 250 255  
 Glu Arg His Arg Arg Gln Gly Arg Glu Val Arg Pro Asp Thr Gln Tyr  
 260 265 270  
 Thr Gly Arg Lys Arg Lys Pro Arg Phe  
 275 280

<210> 229

<211> 525

<212> PRT

<213> Homo sapiens

<400> 229  
 Met Ala Ala Gly Gly Ser Gly Gly Arg Ala Ser Cys Pro Pro Gly Val  
 1 5 10 15  
 Gly Val Gly Pro Gly Thr Gly Gly Ser Pro Gly Pro Ser Ala Asn Ala  
 20 25 30  
 Ala Ala Thr Pro Ala Pro Gly Asn Ala Ala Ala Ala Ala Ala  
 35 40 45  
 Ala Ala Ala Ala Ala Pro Gly Pro Thr Pro Pro Ala Pro Pro Gly  
 50 55 60  
 Pro Gly Thr Asp Ala Gln Ala Ala Gly Ala Glu Arg Ala Glu Glu Ala  
 65 70 75 80  
 Ala Gly Pro Gly Ala Ala Ala Leu Gln Arg Glu Ala Ala Tyr Asn Trp  
 85 90 95

Gln	Ala	Ser	Lys	Pro	Thr	Val	Gln	Glu	Arg	Phe	Ala	Phe	Leu	Phe	Asn
Asn	Glu	Val	Leu	Cys	Asp	Val	His	105	Phe	Leu	Val	Gly	Lys	110	Gly
Ser	Gln	Arg	Ile	Pro	Ala	His	120	Arg	Phe	Val	Leu	Ala	Val	125	Gly
Val	Phe	Asp	Ala	Met	Phe	Asn	Gly	Gly	Met	Ala	Thr	Thr	Ser	Thr	Glu
Ile	Glu	Leu	Pro	Asp	Val	Glu	Pro	Ala	Ala	155	Phe	Leu	Ala	Leu	Leu
Phe	Leu	Tyr	Ser	Asp	Glu	Val	Gln	Ile	Gly	Pro	Glu	Thr	Val	175	Met
Thr	Leu	Tyr	Thr	Ala	Lys	Lys	Tyr	Ala	Val	Pro	Ala	Leu	Glu	190	Ala
Cys	Val	Glu	Phe	Leu	Lys	Lys	200	Asn	Leu	Arg	Ala	Asp	Asn	205	Phe
Leu	Leu	Thr	Gln	Ala	Arg	Leu	Phe	Asp	Glu	Pro	Gln	Leu	Ala	220	Ser
225	Leu	Glu	Asn	Ile	Asp	Lys	Asn	Thr	Ala	235	Asp	Ala	Ile	240	Thr
Cys	Phe	Thr	Asp	Ile	Asp	Leu	Asp	Thr	Leu	Val	Ala	Val	Leu	255	Glu
Gly	Thr	Leu	Gly	Ile	Arg	Glu	Val	Arg	Leu	Phe	Asn	Ala	Val	270	Val
Asp	Thr	Leu	Gly	Ile	Arg	Glu	Val	Arg	Leu	Phe	Asn	Ala	Val	285	Val
Trp	Ser	Glu	Ala	Glu	Cys	Gln	Arg	Gln	Gln	Leu	Gln	Val	Thr	300	Pro
Asn	Arg	Arg	Lys	Val	Leu	Gly	Lys	Ala	Leu	Gly	Leu	Ile	Arg	315	Phe
Leu	Met	Thr	Ile	Glu	Glu	Phe	Ala	Ala	Gly	Pro	Ala	Gln	Ser	330	Gly
Leu	Val	Asp	Arg	Glu	Val	Val	Ser	Leu	Phe	Leu	His	Phe	Thr	335	Val
Pro	Lys	Pro	Arg	Val	Glu	Phe	Ile	Asp	Arg	Pro	Arg	Cys	Cys	350	Leu
Gly	Lys	Glu	Cys	Ser	Ile	Asn	Arg	Phe	Gln	Gln	Val	Glu	Ser	365	Arg
Gly	Tyr	Ser	Gly	Thr	Ser	Asp	Arg	Ile	Arg	Phe	Ser	Val	Asn	380	Lys
Ile	Phe	Val	Val	Gly	Phe	Gly	Leu	Tyr	Gly	Ser	Ile	His	Gly	395	Pro
Asp	Tyr	Gln	Val	Asn	Ile	Gln	Ile	Ile	His	Thr	Asp	Ser	Asn	410	Thr
Leu	Gly	Gln	Asn	Asp	Thr	Gly	Phe	Ser	Cys	Asp	Gly	Ser	Ala	425	Ser
Phe	Arg	Val	Met	Phe	Lys	Glu	Pro	Val	Glu	Val	Leu	Pro	Asn	440	Val
Tyr	Thr	Ala	Cys	Ala	Thr	Leu	Lys	Gly	Pro	Asp	Ser	His	Tyr	455	Gly
Lys	Gly	Leu	Arg	Lys	Val	Thr	His	Glu	Ser	Pro	Thr	Thr	Gly	470	Ala
Thr	Cys	Phe	Thr	Phe	Cys	Tyr	Ala	Ala	Gly	Asn	Asn	Asn	Gly	485	Thr
Val	Glu	Asp	Gly	Gln	Ile	Pro	Glu	Val	Ile	Phe	Tyr	Thr	510	500	Ser
		515					520					525			

&lt;210&gt; 230

&lt;211&gt; 933

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 230

Met Thr Glu Leu Lys Ala Lys Gly Pro Arg Ala Pro His Val Ala Gly  
 1 5 10 15  
 Gly Pro Pro Ser Pro Glu Val Gly Ser Pro Leu Leu Cys Arg Pro Ala  
 20 25 30  
 Ala Gly Pro Phe Pro Gly Ser Gln Thr Ser Asp Thr Leu Pro Glu Val  
 35 40 45  
 Ser Ala Ile Pro Ile Ser Leu Asp Gly Leu Leu Phe Pro Arg Pro Cys  
 50 55 60  
 Gln Gly Gln Asp Pro Ser Asp Glu Lys Thr Gln Asp Gln Gln Ser Leu  
 65 70 75 80  
 Ser Asp Val Glu Gly Ala Tyr Ser Arg Ala Glu Ala Thr Arg Gly Ala  
 85 90 95  
 Gly Gly Ser Ser Ser Ser Pro Pro Glu Lys Asp Ser Gly Leu Leu Asp  
 100 105 110  
 Ser Val Leu Asp Thr Leu Leu Ala Pro Ser Gly Pro Gly Gln Ser Gln  
 115 120 125  
 Pro Ser Pro Pro Ala Cys Glu Val Thr Ser Ser Trp Cys Leu Phe Gly  
 130 135 140  
 Pro Glu Leu Pro Glu Asp Pro Pro Ala Ala Pro Ala Thr Gln Arg Val  
 145 150 155 160  
 Leu Ser Pro Leu Met Ser Arg Ser Gly Cys Lys Val Gly Asp Ser Ser  
 165 170 175  
 Gly Thr Ala Ala Ala His Lys Val Leu Pro Arg Gly Leu Ser Pro Ala  
 180 185 190  
 Arg Gln Leu Leu Leu Pro Ala Ser Glu Ser Pro His Trp Ser Gly Ala  
 195 200 205  
 Pro Val Lys Pro Ser Pro Gln Ala Ala Val Glu Val Glu Glu Glu  
 210 215 220  
 Asp Ser Ser Glu Ser Glu Glu Ser Ala Gly Pro Leu Leu Lys Gly Lys  
 225 230 235 240  
 Pro Arg Ala Leu Gly Gly Ala Ala Ala Gly Gly Gly Ala Ala Ala Cys  
 245 250 255  
 Pro Pro Gly Ala Ala Ala Gly Gly Val Ala Leu Val Pro Lys Glu Asp  
 260 265 270  
 Ser Arg Phe Ser Ala Pro Arg Val Ala Leu Val Glu Gln Asp Ala Pro  
 275 280 285  
 Met Ala Pro Gly Arg Ser Pro Leu Ala Thr Thr Val Met Asp Phe Ile  
 290 295 300  
 His Val Pro Ile Leu Pro Leu Asn His Ala Leu Leu Ala Ala Arg Thr  
 305 310 315 320  
 Arg Gln Leu Leu Glu Asp Glu Ser Tyr Asp Gly Gly Ala Gly Ala Ala  
 325 330 335  
 Ser Ala Phe Ala Pro Pro Arg Thr Ser Pro Cys Ala Ser Ser Thr Pro  
 340 345 350  
 Val Ala Val Gly Asp Phe Pro Asp Cys Ala Tyr Pro Pro Asp Ala Glu  
 355 360 365  
 Pro Lys Asp Asp Ala Tyr Pro Leu Tyr Ser Asp Phe Gln Pro Pro Ala  
 370 375 380  
 Leu Lys Ile Lys Glu Glu Glu Gly Ala Glu Ala Ser Ala Arg Ser  
 385 390 395 400

Pro	Arg	Ser	Tyr	Leu	Val	Ala	Gly	Ala	Asn	Pro	Ala	Ala	Phe	Pro	Asp
				405					410					415	
Phe	Pro	Leu	Gly	Pro	Pro	Pro	Pro	Leu	Pro	Pro	Arg	Ala	Thr	Pro	Ser
			420					425					430		
Arg	Pro	Gly	Glu	Ala	Ala	Val	Thr	Ala	Ala	Pro	Ala	Ser	Ala	Ser	Val
		435					440					445			
Ser	Ser	Ala	Ser	Ser	Ser	Gly	Ser	Thr	Leu	Glu	Cys	Ile	Leu	Tyr	Lys
	450					455					460				
Ala	Glu	Gly	Ala	Pro	Pro	Gln	Gln	Gly	Pro	Phe	Ala	Pro	Pro	Pro	Cys
465					470					475					480
Lys	Ala	Pro	Gly	Ala	Ser	Gly	Cys	Leu	Leu	Pro	Arg	Asp	Gly	Leu	Pro
				485					490					495	
Ser	Thr	Ser	Ala	Ser	Ala	Ala	Ala	Ala	Gly	Ala	Ala	Pro	Ala	Leu	Tyr
			500					505					510		
Pro	Ala	Leu	Gly	Leu	Asn	Gly	Leu	Pro	Gln	Leu	Gly	Tyr	Gln	Ala	Ala
		515					520					525			
Val	Leu	Lys	Glu	Gly	Leu	Pro	Gln	Val	Tyr	Pro	Pro	Tyr	Leu	Asn	Tyr
	530					535					540				
Leu	Arg	Pro	Asp	Ser	Glu	Ala	Ser	Gln	Ser	Pro	Gln	Tyr	Ser	Phe	Glu
545					550					555					560
Ser	Leu	Pro	Gln	Lys	Ile	Cys	Leu	Ile	Cys	Gly	Asp	Glu	Ala	Ser	Gly
				565					570						575
Cys	His	Tyr	Gly	Val	Leu	Thr	Cys	Gly	Ser	Cys	Lys	Val	Phe	Phe	Lys
			580					585					590		
Arg	Ala	Met	Glu	Gly	Gln	His	Asn	Tyr	Leu	Cys	Ala	Gly	Arg	Asn	Asp
		595					600					605			
Cys	Ile	Val	Asp	Lys	Ile	Arg	Arg	Lys	Asn	Cys	Pro	Ala	Cys	Arg	Leu
	610					615					620				
Arg	Lys	Cys	Cys	Gln	Ala	Gly	Met	Val	Leu	Gly	Gly	Arg	Lys	Phe	Lys
625					630					635					640
Lys	Phe	Asn	Lys	Val	Arg	Val	Val	Arg	Ala	Leu	Asp	Ala	Val	Ala	Leu
				645					650					655	
Pro	Gln	Pro	Leu	Gly	Val	Pro	Asn	Glu	Ser	Gln	Ala	Leu	Ser	Gln	Arg
			660					665					670		
Phe	Thr	Phe	Ser	Pro	Gly	Gln	Asp	Ile	Gln	Leu	Ile	Pro	Pro	Leu	Ile
		675					680					685			
Asn	Leu	Leu	Met	Ser	Ile	Glu	Pro	Asp	Val	Ile	Tyr	Ala	Gly	His	Asp
	690					695					700				
Asn	Thr	Lys	Pro	Asp	Thr	Ser	Ser	Ser	Leu	Leu	Thr	Ser	Leu	Asn	Gln
705					710					715					720
Leu	Gly	Glu	Arg	Gln	Leu	Leu	Ser	Val	Val	Lys	Trp	Ser	Lys	Ser	Leu
				725					730					735	
Pro	Gly	Phe	Arg	Asn	Leu	His	Ile	Asp	Asp	Gln	Ile	Thr	Leu	Ile	Gln
			740					745					750		
Tyr	Ser	Trp	Met	Ser	Leu	Met	Val	Phe	Gly	Leu	Gly	Trp	Arg	Ser	Tyr
		755					760					765			
Lys	His	Val	Ser	Gly	Gln	Met	Leu	Tyr	Phe	Ala	Pro	Asp	Leu	Ile	Leu
	770					775					780				
Asn	Glu	Gln	Arg	Met	Lys	Glu	Ser	Ser	Phe	Tyr	Ser	Leu	Cys	Leu	Thr
785					790					795					800
Met	Trp	Gln	Ile	Pro	Gln	Glu	Phe	Val	Lys	Leu	Gln	Val	Ser	Gln	Glu
				805					810					815	
Glu	Phe	Leu	Cys	Met	Lys	Val	Leu	Leu	Leu	Leu	Asn	Thr	Ile	Pro	Leu
			820					825					830		
Glu	Gly	Leu	Arg	Ser	Gln	Thr	Gln	Phe	Glu	Glu	Met	Arg	Ser	Ser	Tyr
		835					840					845			
Ile	Arg	Glu	Leu	Ile	Lys	Ala	Ile	Gly	Leu	Arg	Gln	Lys	Gly	Val	Val
	850					855					860				
Ser	Ser	Ser	Gln	Arg	Phe	Tyr	Gln	Leu	Thr	Lys	Leu	Leu	Asp	Asn	Leu
865					870					875					880
His	Asp	Leu	Val	Lys	Gln	Leu	His	Leu	Tyr	Cys	Leu	Asn	Thr	Phe	Ile
				885					890					895	



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Gln Ser Arg Ala Leu Ser Val Glu Phe Pro Glu Met Met Ser Glu Val  
 900 905 910  
 Ile Ala Ala Gln Leu Pro Lys Ile Leu Ala Gly Met Val Lys Pro Leu  
 915 920 925  
 Leu Phe His Lys Lys  
 930

&lt;210&gt; 231

&lt;211&gt; 186

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 231  
 Met Asp Ala Asp Ser Asp Val Ala Leu Asp Ile Leu Ile Thr Asn Val  
 1 5 10 15  
 Val Cys Val Phe Arg Thr Arg Cys His Leu Asn Leu Arg Lys Ile Ala  
 20 25 30  
 Leu Glu Gly Ala Asn Val Ile Tyr Lys Arg Asp Val Gly Lys Val Leu  
 35 40 45  
 Met Lys Leu Arg Lys Pro Arg Ile Thr Ala Thr Ile Trp Ser Ser Gly  
 50 55 60  
 Lys Ile Ile Cys Thr Gly Ala Thr Ser Glu Glu Glu Ala Lys Phe Gly  
 65 70 75 80  
 Ala Arg Arg Leu Ala Arg Ser Leu Gln Lys Leu Gly Phe Gln Val Ile  
 85 90 95  
 Phe Thr Asp Phe Lys Val Val Asn Val Leu Ala Val Cys Asn Met Pro  
 100 105 110  
 Phe Glu Ile Arg Leu Pro Glu Phe Thr Lys Asn Asn Arg Pro His Ala  
 115 120 125  
 Ser Tyr Glu Pro Glu Leu His Pro Ala Val Cys Tyr Arg Ile Lys Ser  
 130 135 140  
 Leu Arg Ala Thr Leu Gln Ile Phe Ser Thr Gly Ser Ile Thr Val Thr  
 145 150 155 160  
 Gly Pro Asn Val Lys Ala Val Ala Thr Ala Val Glu Gln Ile Tyr Pro  
 165 170 175  
 Phe Val Phe Glu Ser Arg Lys Glu Ile Leu  
 180 185

&lt;210&gt; 232

&lt;211&gt; 1744

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 232  
 Met Arg Leu Leu Trp Gly Leu Ile Trp Ala Ser Ser Phe Phe Thr Leu  
 1 5 10 15  
 Ser Leu Gln Lys Pro Arg Leu Leu Leu Phe Ser Pro Ser Val Val His  
 20 25 30  
 Leu Gly Val Pro Leu Ser Val Gly Val Gln Leu Gln Asp Val Pro Arg  
 35 40 45  
 Gly Gln Val Val Lys Gly Ser Val Phe Leu Arg Asn Pro Ser Arg Asn  
 50 55 60

Asn	Val	Pro	Cys	Ser	Pro	Lys	Val	Asp	Phe	Thr	Leu	Ser	Ser	Glu	Arg
65					70					75					80
Asp	Phe	Ala	Leu	Leu	Ser	Leu	Gln	Val	Pro	Leu	Lys	Asp	Ala	Lys	Ser
				85					90					95	
Cys	Gly	Leu	His	Gln	Leu	Leu	Arg	Gly	Pro	Glu	Val	Gln	Leu	Val	Ala
			100					105					110		
His	Ser	Pro	Trp	Leu	Lys	Asp	Ser	Leu	Ser	Arg	Thr	Thr	Asn	Ile	Gln
		115					120					125			
Gly	Ile	Asn	Leu	Leu	Phe	Ser	Ser	Arg	Arg	Gly	His	Leu	Phe	Leu	Gln
	130					135					140				
Thr	Asp	Gln	Pro	Ile	Tyr	Asn	Pro	Gly	Gln	Arg	Val	Arg	Tyr	Arg	Val
145					150					155					160
Phe	Ala	Leu	Asp	Gln	Lys	Met	Arg	Pro	Ser	Thr	Asp	Thr	Ile	Thr	Val
				165					170					175	
Met	Val	Glu	Asn	Ser	His	Gly	Leu	Arg	Val	Arg	Lys	Lys	Glu	Val	Tyr
			180					185					190		
Met	Pro	Ser	Ser	Ile	Phe	Gln	Asp	Asp	Phe	Val	Ile	Pro	Asp	Ile	Ser
		195					200					205			
Glu	Pro	Gly	Thr	Trp	Lys	Ile	Ser	Ala	Arg	Phe	Ser	Asp	Gly	Leu	Glu
	210					215						220			
Ser	Asn	Ser	Ser	Thr	Gln	Phe	Glu	Val	Lys	Lys	Tyr	Val	Leu	Pro	Asn
225					230					235					240
Phe	Glu	Val	Lys	Ile	Thr	Pro	Gly	Lys	Pro	Tyr	Ile	Leu	Thr	Val	Pro
				245					250					255	
Gly	His	Leu	Asp	Glu	Met	Gln	Leu	Asp	Ile	Gln	Ala	Arg	Tyr	Ile	Tyr
			260					265					270		
Gly	Lys	Pro	Val	Gln	Gly	Val	Ala	Tyr	Val	Arg	Phe	Gly	Leu	Leu	Asp
		275					280					285			
Glu	Asp	Gly	Lys	Lys	Thr	Phe	Phe	Arg	Gly	Leu	Glu	Ser	Gln	Thr	Lys
	290					295					300				
Leu	Val	Asn	Gly	Gln	Ser	His	Ile	Ser	Leu	Ser	Lys	Ala	Glu	Phe	Gln
305					310					315					320
Asp	Ala	Leu	Glu	Lys	Leu	Asn	Met	Gly	Ile	Thr	Asp	Leu	Gln	Gly	Leu
				325					330					335	
Arg	Leu	Tyr	Val	Ala	Ala	Ala	Ile	Ile	Glu	Tyr	Pro	Gly	Gly	Glu	Met
			340					345					350		
Glu	Glu	Ala	Glu	Leu	Thr	Ser	Trp	Tyr	Phe	Val	Ser	Ser	Pro	Phe	Ser
		355					360					365			
Leu	Asp	Leu	Ser	Lys	Thr	Lys	Arg	His	Leu	Val	Pro	Gly	Ala	Pro	Phe
	370					375					380				
Leu	Leu	Gln	Ala	Leu	Val	Arg	Glu	Met	Ser	Gly	Ser	Pro	Ala	Ser	Gly
385					390					395					400
Ile	Pro	Val	Lys	Val	Ser	Ala	Thr	Val	Ser	Ser	Pro	Gly	Ser	Val	Pro
				405						410				415	
Glu	Val	Gln	Asp	Ile	Gln	Gln	Asn	Thr	Asp	Gly	Ser	Gly	Gln	Val	Ser
			420					425					430		
Ile	Pro	Ile	Ile	Ile	Pro	Gln	Thr	Ile	Ser	Glu	Leu	Gln	Leu	Ser	Val
		435					440					445			
Ser	Ala	Gly	Ser	Pro	His	Pro	Ala	Ile	Ala	Arg	Leu	Thr	Val	Ala	Ala
	450					455					460				
Pro	Pro	Ser	Gly	Gly	Pro	Gly	Phe	Leu	Ser	Ile	Glu	Arg	Pro	Asp	Ser
465					470					475					480
Arg	Pro	Pro	Arg	Val	Gly	Asp	Thr	Leu	Asn	Leu	Asn	Leu	Arg	Ala	Val
				485					490					495	
Gly	Ser	Gly	Ala	Thr	Phe	Ser	His	Tyr	Tyr	Tyr	Met	Ile	Leu	Ser	Arg
			500					505					510		
Gly	Gln	Ile	Val	Phe	Met	Asn	Arg	Glu	Pro	Lys	Arg	Thr	Leu	Thr	Ser
		515					520					525			
Val	Ser	Val	Phe	Val	Asp	His	His	Leu	Ala	Pro	Ser	Phe	Tyr	Phe	Val
	530					535					540				
Ala	Phe	Tyr	Tyr	His	Gly	Asp	His	Pro	Val	Ala	Asn	Ser	Leu	Arg	Val
545					550					555					560

Asp Val Gln Ala Gly Ala Cys Glu Gly Lys Leu Glu Leu Ser Val Asp  
 565 570 575  
 Gly Ala Lys Gln Tyr Arg Asn Gly Glu Ser Val Lys Leu His Leu Glu  
 580 585 590  
 Thr Asp Ser Leu Ala Leu Val Ala Leu Gly Ala Leu Asp Thr Ala Leu  
 595 600 605  
 Tyr Ala Ala Gly Ser Lys Ser His Lys Pro Leu Asn Met Gly Lys Val  
 610 615 620  
 Phe Glu Ala Met Asn Ser Tyr Asp Leu Gly Cys Gly Pro Gly Gly Gly  
 625 630 635 640  
 Asp Ser Ala Leu Gln Val Phe Gln Ala Ala Gly Leu Ala Phe Ser Asp  
 645 650 655  
 Gly Asp Gln Trp Thr Leu Ser Arg Lys Arg Leu Ser Cys Pro Lys Glu  
 660 665 670  
 Lys Thr Thr Arg Lys Lys Arg Asn Val Asn Phe Gln Lys Ala Ile Asn  
 675 680 685  
 Glu Lys Leu Gly Gln Tyr Ala Ser Pro Thr Ala Lys Arg Cys Cys Gln  
 690 695 700  
 Asp Gly Val Thr Arg Leu Pro Met Met Arg Ser Cys Glu Gln Arg Ala  
 705 710 715 720  
 Ala Arg Val Gln Gln Pro Asp Cys Arg Glu Pro Phe Leu Ser Cys Cys  
 725 730 735  
 Gln Phe Ala Glu Ser Leu Arg Lys Lys Ser Arg Asp Lys Gly Gln Ala  
 740 745 750  
 Gly Leu Gln Arg Ala Leu Glu Ile Leu Gln Glu Glu Asp Leu Ile Asp  
 755 760 765  
 Glu Asp Asp Ile Pro Val Arg Ser Phe Phe Pro Glu Asn Trp Leu Trp  
 770 775 780  
 Arg Val Glu Thr Val Asp Arg Phe Gln Ile Leu Thr Leu Trp Leu Pro  
 785 790 795 800  
 Asp Ser Leu Thr Thr Trp Glu Ile His Gly Leu Ser Leu Ser Lys Thr  
 805 810 815  
 Lys Gly Leu Cys Val Ala Thr Pro Val Gln Leu Arg Val Phe Arg Glu  
 820 825 830  
 Phe His Leu His Leu Arg Leu Pro Met Ser Val Arg Arg Phe Glu Gln  
 835 840 845  
 Leu Glu Leu Arg Pro Val Leu Tyr Asn Tyr Leu Asp Lys Asn Leu Thr  
 850 855 860  
 Val Ser Val His Val Ser Pro Val Glu Gly Leu Cys Leu Ala Gly Gly  
 865 870 875 880  
 Gly Gly Leu Ala Gln Gln Val Leu Val Pro Ala Gly Ser Ala Arg Pro  
 885 890 895  
 Val Ala Phe Ser Val Val Pro Thr Ala Ala Ala Val Ser Leu Lys  
 900 905 910  
 Val Val Ala Arg Gly Ser Phe Glu Phe Pro Val Gly Asp Ala Val Ser  
 915 920 925  
 Lys Val Leu Gln Ile Glu Lys Glu Gly Ala Ile His Arg Glu Glu Leu  
 930 935 940  
 Val Tyr Glu Leu Asn Pro Leu Asp His Arg Gly Arg Thr Leu Glu Ile  
 945 950 955 960  
 Pro Gly Asn Ser Asp Pro Asn Met Ile Pro Asp Gly Asp Phe Asn Ser  
 965 970 975  
 Tyr Val Arg Val Thr Ala Ser Asp Pro Leu Asp Thr Leu Gly Ser Glu  
 980 985 990  
 Gly Ala Leu Ser Pro Gly Gly Val Ala Ser Leu Leu Arg Leu Pro Arg  
 995 1000 1005  
 Gly Cys Gly Glu Gln Thr Met Ile Tyr Leu Ala Pro Thr Leu Ala  
 1010 1015 1020  
 Ala Ser Arg Tyr Leu Asp Lys Thr Glu Gln Trp Ser Thr Leu Pro  
 1025 1030 1035  
 Pro Glu Thr Lys Asp His Ala Val Asp Leu Ile Gln Lys Gly Tyr  
 1040 1045 1050

Met	Arg	Ile	Gln	Gln	Phe	Arg	Lys	Ala	Asp	Gly	Ser	Tyr	Ala	Ala
1055						1060					1065			
Trp	Leu	Ser	Arg	Gly	Ser	Ser	Thr	Trp	Leu	Thr	Ala	Phe	Val	Leu
1070						1075					1080			
Lys	Val	Leu	Ser	Leu	Ala	Gln	Glu	Gln	Val	Gly	Gly	Ser	Pro	Glu
1085						1090					1095			
Lys	Leu	Gln	Glu	Thr	Ser	Asn	Trp	Leu	Leu	Ser	Gln	Gln	Gln	Ala
1100						1105					1110			
Asp	Gly	Ser	Phe	Gln	Asp	Leu	Ser	Pro	Val	Ile	His	Arg	Ser	Met
1115						1120					1125			
Gln	Gly	Gly	Leu	Val	Gly	Asn	Asp	Glu	Thr	Val	Ala	Leu	Thr	Ala
1130						1135					1140			
Phe	Val	Thr	Ile	Ala	Leu	His	His	Gly	Leu	Ala	Val	Phe	Gln	Asp
1145						1150					1155			
Glu	Gly	Ala	Glu	Pro	Leu	Lys	Gln	Arg	Val	Glu	Ala	Ser	Ile	Ser
1160						1165					1170			
Lys	Ala	Ser	Ser	Phe	Leu	Gly	Glu	Lys	Ala	Ser	Ala	Gly	Leu	Leu
1175						1180					1185			
Gly	Ala	His	Ala	Ala	Ala	Ile	Thr	Ala	Tyr	Ala	Leu	Thr	Leu	Thr
1190						1195					1200			
Lys	Ala	Pro	Ala	Asp	Leu	Arg	Gly	Val	Ala	His	Asn	Asn	Leu	Met
1205						1210					1215			
Ala	Met	Ala	Gln	Glu	Thr	Gly	Asp	Asn	Leu	Tyr	Trp	Gly	Ser	Val
1220						1225					1230			
Thr	Gly	Ser	Gln	Ser	Asn	Ala	Val	Ser	Pro	Thr	Pro	Ala	Pro	Arg
1235						1240					1245			
Asn	Pro	Ser	Asp	Pro	Met	Pro	Gln	Ala	Pro	Ala	Leu	Trp	Ile	Glu
1250						1255					1260			
Thr	Thr	Ala	Tyr	Ala	Leu	Leu	His	Leu	Leu	Leu	His	Glu	Gly	Lys
1265						1270					1275			
Ala	Glu	Met	Ala	Asp	Gln	Ala	Ala	Ala	Trp	Leu	Thr	Arg	Gln	Gly
1280						1285					1290			
Ser	Phe	Gln	Gly	Gly	Phe	Arg	Ser	Thr	Gln	Asp	Thr	Val	Ile	Ala
1295						1300					1305			
Leu	Asp	Ala	Leu	Ser	Ala	Tyr	Trp	Ile	Ala	Ser	His	Thr	Thr	Glu
1310						1315					1320			
Glu	Arg	Gly	Leu	Asn	Val	Thr	Leu	Ser	Ser	Thr	Gly	Arg	Asn	Gly
1325						1330					1335			
Phe	Lys	Ser	His	Ala	Leu	Gln	Leu	Asn	Asn	Arg	Gln	Ile	Arg	Gly
1340						1345					1350			
Leu	Glu	Glu	Glu	Leu	Gln	Phe	Ser	Leu	Gly	Ser	Lys	Ile	Asn	Val
1355						1360					1365			
Lys	Val	Gly	Gly	Asn	Ser	Lys	Gly	Thr	Leu	Lys	Val	Leu	Arg	Thr
1370						1375					1380			
Tyr	Asn	Val	Leu	Asp	Met	Lys	Asn	Thr	Thr	Cys	Gln	Asp	Leu	Gln
1385						1390					1395			
Ile	Glu	Val	Thr	Val	Lys	Gly	His	Val	Glu	Tyr	Thr	Met	Glu	Ala
1400						1405					1410			
Asn	Glu	Asp	Tyr	Glu	Asp	Tyr	Glu	Tyr	Asp	Glu	Leu	Pro	Ala	Lys
1415						1420					1425			
Asp	Asp	Pro	Asp	Ala	Pro	Leu	Gln	Pro	Val	Thr	Pro	Leu	Gln	Leu
1430						1435					1440			
Phe	Glu	Gly	Arg	Arg	Asn	Arg	Arg	Arg	Arg	Glu	Ala	Pro	Lys	Val
1445						1450					1455			
Val	Glu	Glu	Gln	Glu	Ser	Arg	Val	His	Tyr	Thr	Val	Cys	Ile	Trp
1460						1465					1470			
Arg	Asn	Gly	Lys	Val	Gly	Leu	Ser	Gly	Met	Ala	Ile	Ala	Asp	Val
1475						1480					1485			
Thr	Leu	Leu	Ser	Gly	Phe	His	Ala	Leu	Arg	Ala	Asp	Leu	Glu	Lys
1490						1495					1500			
Leu	Thr	Ser	Leu	Ser	Asp	Arg	Tyr	Val	Ser	His	Phe	Glu	Thr	Glu
1505						1510					1515			

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[illegible]

**<210> 233**

**<211> 295**

<212> PRT

<213> Homo sapiens

<400>	233																		
Met	Ile	Glu	Val	Leu	Thr	Thr	Thr	Asp	Ser	Gln	Lys	Leu	Leu	His	Gln				
1				5					10					15					
Leu	Asn	Ala	Leu	Leu	Glu	Gln	Glu	Ser	Arg	Cys	Gln	Pro	Lys	Val	Cys				
			20					25					30						
Gly	Leu	Arg	Leu	Ile	Glu	Ser	Ala	His	Asp	Asn	Gly	Leu	Arg	Met	Thr				
			35				40					45							
Ala	Arg	Leu	Arg	Asp	Phe	Glu	Val	Lys	Asp	Leu	Leu	Ser	Leu	Thr	Gln				
			50			55					60								
Phe	Phe	Gly	Phe	Asp	Thr	Glu	Thr	Phe	Ser	Leu	Ala	Val	Asn	Leu	Leu				
65					70					75									
Asp	Arg	Phe	Leu	Ser	Lys	Met	Lys	Val	Gln	Pro	Lys	His	Leu	Gly	Cys				
				85					90					95					
Val	Gly	Leu	Ser	Cys	Phe	Tyr	Leu	Ala	Val	Lys	Ser	Ile	Glu	Glu	Glu				
				100				105						110					
Arg	Asn	Val	Pro	Leu	Ala	Thr	Asp	Leu	Ile	Arg	Ile	Ser	Gln	Tyr	Arg				
			115				120					125							
Phe	Thr	Val	Ser	Asp	Leu	Met	Arg	Met	Glu	Lys	Ile	Val	Leu	Glu	Lys				
			130			135						140							

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Val Cys Trp Lys Val Lys Ala Thr Thr Ala Phe Gln Phe Leu Gln Leu  
 145 150 155 160  
 Tyr Tyr Ser Leu Leu Gln Glu Asn Leu Pro Leu Glu Arg Arg Asn Ser  
 165 170 175  
 Ile Asn Phe Glu Arg Leu Glu Ala Gln Leu Lys Ala Cys His Cys Arg  
 180 185 190  
 Ile Ile Phe Ser Lys Ala Lys Pro Ser Val Leu Ala Leu Ser Ile Ile  
 195 200 205  
 Ala Leu Glu Ile Gln Ala Gln Lys Cys Val Glu Leu Thr Glu Gly Ile  
 210 215 220  
 Glu Cys Leu Gln Lys His Ser Lys Ile Asn Gly Arg Asp Leu Thr Phe  
 225 230 235 240  
 Trp Gln Glu Leu Val Ser Lys Cys Leu Thr Glu Tyr Ser Ser Asn Lys  
 245 250 255  
 Cys Ser Lys Pro Asn Val Gln Lys Leu Lys Trp Ile Val Ser Gly Arg  
 260 265 270  
 Thr Ala Arg Gln Leu Lys His Ser Tyr Tyr Arg Ile Thr His Leu Pro  
 275 280 285  
 Thr Ile Pro Glu Met Val Pro  
 290 295

&lt;210&gt; 234

&lt;211&gt; 359

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 234  
 Met Ala Ala Val Ser Gly Leu Val Arg Arg Pro Leu Arg Glu Val Ser  
 1 5 10 15  
 Gly Leu Leu Lys Arg Arg Phe His Trp Thr Ala Pro Ala Ala Leu Gln  
 20 25 30  
 Val Thr Val Arg Asp Ala Ile Asn Gln Gly Met Asp Glu Glu Leu Glu  
 35 40 45  
 Arg Asp Glu Lys Val Phe Leu Leu Gly Glu Glu Val Ala Gln Tyr Asp  
 50 55 60  
 Gly Ala Tyr Lys Val Ser Arg Gly Leu Trp Lys Lys Tyr Gly Asp Lys  
 65 70 75 80  
 Arg Ile Ile Asp Thr Pro Ile Ser Glu Met Gly Phe Ala Gly Ile Ala  
 85 90 95  
 Val Gly Ala Ala Met Ala Gly Leu Arg Pro Ile Cys Glu Phe Met Thr  
 100 105 110  
 Phe Asn Phe Ser Met Gln Ala Ile Asp Gln Val Ile Asn Ser Ala Ala  
 115 120 125  
 Lys Thr Tyr Tyr Met Ser Gly Gly Leu Gln Pro Val Pro Ile Val Phe  
 130 135 140  
 Arg Gly Pro Asn Gly Ala Ser Ala Gly Val Ala Ala Gln His Ser Gln  
 145 150 155 160  
 Cys Phe Ala Ala Trp Tyr Gly His Cys Pro Gly Leu Lys Val Val Ser  
 165 170 175  
 Pro Trp Asn Ser Glu Asp Ala Lys Gly Leu Ile Lys Ser Ala Ile Arg  
 180 185 190  
 Asp Asn Asn Pro Val Val Val Leu Glu Asn Glu Leu Met Tyr Gly Val  
 195 200 205  
 Pro Phe Glu Phe Leu Pro Glu Ala Gln Ser Lys Asp Phe Leu Ile Pro  
 210 215 220  
 Ile Gly Lys Ala Lys Ile Glu Arg Gln Gly Thr His Ile Thr Val Val  
 225 230 235 240

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Ser His Ser Arg Pro Val Gly His Cys Leu Glu Ala Ala Ala Val Leu  
 245 250 255  
 Ser Lys Glu Gly Val Glu Cys Glu Val Ile Asn Met Arg Thr Ile Arg  
 260 265 270  
 Pro Met Asp Met Glu Thr Ile Glu Ala Ser Val Met Lys Thr Asn His  
 275 280 285  
 Leu Val Thr Val Glu Gly Gly Trp Pro Gln Phe Gly Val Gly Ala Glu  
 290 295 300  
 Ile Cys Ala Arg Ile Met Glu Gly Pro Ala Phe Asn Phe Leu Asp Ala  
 305 310 315 320  
 Pro Ala Val Arg Val Thr Gly Ala Asp Val Pro Met Pro Tyr Ala Lys  
 325 330 335  
 Ile Leu Glu Asp Asn Ser Ile Pro Gln Val Lys Asp Ile Ile Phe Ala  
 340 345 350  
 Ile Lys Lys Thr Leu Asn Ile  
 355

&lt;210&gt; 235

&lt;211&gt; 420

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 235  
 Met Glu Val Pro Pro Arg Leu Ser His Val Pro Pro Pro Leu Phe Pro  
 1 5 10 15  
 Ser Ala Pro Ala Thr Leu Ala Ser Arg Ser Leu Ser His Trp Arg Pro  
 20 25 30  
 Arg Pro Pro Arg Gln Leu Ala Pro Leu Leu Pro Ser Leu Ala Pro Ser  
 35 40 45  
 Ser Ala Arg Gln Gly Ala Arg Arg Ala Gln Arg His Val Thr Ala Gln  
 50 55 60  
 Gln Pro Ser Arg Leu Ala Gly Gly Ala Ala Ile Lys Gly Gly Arg Arg  
 65 70 75 80  
 Arg Arg Pro Asp Leu Phe Arg Arg His Phe Lys Ser Ser Ser Ile Gln  
 85 90 95  
 Arg Ser Ala Ala Ala Ala Ala Thr Arg Thr Ala Arg Gln His Pro  
 100 105 110  
 Pro Ala Asp Ser Ser Val Thr Met Glu Asp Met Asn Glu Tyr Ser Asn  
 115 120 125  
 Ile Glu Glu Phe Ala Glu Gly Ser Lys Ile Asn Ala Ser Lys Asn Gln  
 130 135 140  
 Gln Asp Asp Gly Lys Met Phe Ile Gly Gly Leu Ser Trp Asp Thr Ser  
 145 150 155 160  
 Lys Lys Asp Leu Thr Glu Tyr Leu Ser Arg Phe Gly Glu Val Val Asp  
 165 170 175  
 Cys Thr Ile Lys Thr Asp Pro Val Thr Gly Arg Ser Arg Gly Phe Gly  
 180 185 190  
 Phe Val Leu Phe Lys Asp Ala Ala Ser Val Asp Lys Val Leu Glu Leu  
 195 200 205  
 Lys Glu His Lys Leu Asp Gly Lys Leu Ile Asp Pro Lys Arg Ala Lys  
 210 215 220  
 Ala Leu Lys Gly Lys Glu Pro Pro Lys Lys Val Phe Val Gly Gly Leu  
 225 230 235 240  
 Ser Pro Asp Thr Ser Glu Glu Gln Ile Lys Glu Tyr Phe Gly Ala Phe  
 245 250 255  
 Gly Glu Ile Glu Asn Ile Glu Leu Pro Met Asp Thr Lys Thr Asn Glu  
 260 265 270

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Arg Arg Gly Phe Cys Phe Ile Thr Tyr Thr Asp Glu Glu Pro Val Lys  
 275 280 285  
 Lys Leu Leu Glu Ser Arg Tyr His Gln Ile Gly Ser Gly Lys Cys Glu  
 290 295 300  
 Ile Lys Val Ala Gln Pro Lys Glu Val Tyr Arg Gln Gln Gln Gln  
 305 310 315 320  
 Gln Lys Gly Gly Arg Gly Ala Ala Ala Gly Gly Arg Gly Gly Thr Arg  
 325 330 335  
 Gly Arg Gly Arg Gly Gln Gly Gln Asn Trp Asn Gln Gly Phe Asn Asn  
 340 345 350  
 Tyr Tyr Asp Gln Gly Tyr Gly Asn Tyr Asn Ser Ala Tyr Gly Gly Asp  
 355 360 365  
 Gln Asn Tyr Ser Gly Tyr Gly Gly Tyr Asp Tyr Thr Gly Tyr Asn Tyr  
 370 375 380  
 Gly Asn Tyr Gly Tyr Gly Gln Gly Tyr Ala Asp Tyr Ser Gly Gln Gln  
 385 390 400  
 Ser Thr Tyr Gly Lys Ala Ser Arg Gly Gly Asn His Gln Asn Asn  
 405 410 415  
 Tyr Gln Pro Tyr  
 420

&lt;210&gt; 236

&lt;211&gt; 211

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 236

Met Asp Asp Ala His Glu Ser Pro Ser Asp Lys Gly Gly Glu Thr Gly  
 1 5 10 15  
 Glu Ser Asp Glu Thr Ala Ala Val Pro Gly Asp Pro Gly Ala Thr Asp  
 20 25 30  
 Thr Asp Gly Ile Pro Glu Glu Thr Asp Gly Asp Ala Asp Val Asp Leu  
 35 40 45  
 Lys Glu Ala Ala Ala Glu Glu Gly Glu Leu Glu Ser Gln Asp Val Ser  
 50 55 60  
 Asp Leu Thr Thr Val Glu Arg Glu Asp Ser Ser Leu Leu Asn Pro Ala  
 65 70 75 80  
 Ala Lys Lys Leu Lys Ile Asp Thr Lys Glu Lys Lys Glu Lys Lys Gln  
 85 90 95  
 Lys Val Asp Glu Asp Glu Ile Gln Lys Met Gln Ile Leu Val Ser Ser  
 100 105 110  
 Phe Ser Glu Glu Gln Leu Asn Arg Tyr Glu Met Tyr Arg Arg Ser Ala  
 115 120 125  
 Phe Pro Lys Ala Ala Ile Lys Arg Leu Ile Gln Ser Ile Thr Gly Thr  
 130 135 140  
 Ser Val Ser Gln Asn Val Val Ile Ala Met Ser Gly Ile Ser Lys Val  
 145 150 155 160  
 Phe Val Gly Glu Val Val Glu Glu Ala Leu Asp Val Cys Glu Lys Trp  
 165 170 175  
 Gly Glu Met Pro Pro Leu Gln Pro Lys His Met Arg Glu Ala Val Arg  
 180 185 190  
 Arg Leu Lys Ser Lys Gly Gln Ile Pro Asn Ser Lys His Lys Lys Ile  
 195 200 205  
 Ile Phe Phe  
 210



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&lt;210&gt; 237

&lt;211&gt; 382

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (19)..(19)

&lt;223&gt; X = A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y

&lt;400&gt; 237

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Met Ala Leu Gln Gly Ile Ser Val Val Glu Leu Ser Gly Leu Ala Pro
1      5      10      15
Gly Arg Xaa Cys Ala Met Val Leu Ala Asp Phe Gly Ala Arg Val Val
20      25      30
Arg Val Asp Arg Pro Gly Ser Arg Tyr Asp Val Ser Arg Leu Gly Arg
35      40      45
Gly Lys Arg Ser Leu Val Leu Asp Leu Lys Gln Pro Arg Glu Pro Arg
50      55      60
Ala Ala Ala Ser Val Gln Ala Val Gly Cys Ala Ala Gly Ala Leu Pro
65      70      75      80
Pro Arg Cys His Gly Glu Thr Pro Ala Gly Pro Arg Asp Ser Ala Ala
85      90      95
Gly Lys Ser Lys Ala Tyr Leu Cys Gln Ala Glu Trp Ile Trp Pro Val
100      105      110
Gln Glu Ser Phe Cys Arg Leu Ala Gly His Asp Ile Asn Tyr Leu Ala
115      120      125
Leu Ser Gly Val Leu Ser Lys Ile Gly Arg Ser Gly Glu Asn Pro Tyr
130      135      140
Ala Pro Leu Asn Leu Val Ala Asp Phe Ala Gly Gly Leu Met Cys
145      150      155      160
Ala Leu Gly Ile Ile Met Ala Leu Phe Asp Arg Thr Arg Thr Asp Lys
165      170      175
Gly Gln Val Ile Asp Ala Asn Met Val Glu Gly Thr Ala Tyr Leu Ser
180      185      190
Ser Phe Leu Trp Lys Thr Gln Lys Ser Ser Leu Trp Glu Ala Pro Arg
195      200      205
Gly Gln Asn Met Leu Asp Gly Gly Ala Pro Phe Tyr Thr Thr Tyr Arg
210      215      220
Thr Ala Asp Gly Glu Phe Met Ala Val Gly Ala Ile Glu Pro Gln Phe
225      230      235      240
Tyr Glu Leu Leu Ile Lys Gly Leu Gly Leu Lys Ser Asp Glu Leu Pro
245      250      255
Asn Gln Met Ser Thr Asp Asp Trp Pro Glu Met Lys Lys Lys Phe Ala
260      265      270
Asp Val Phe Ala Lys Lys Thr Lys Ala Glu Trp Cys Gln Ile Phe Asp
275      280      285
Gly Thr Asp Ala Cys Val Thr Pro Val Leu Thr Phe Glu Glu Val Val
290      295      300
His His Asp His Asn Lys Glu Arg Gly Ser Phe Ile Thr Ser Glu Glu
305      310      315      320
Gln Asp Val Ser Pro Arg Leu Ala Pro Leu Leu Leu Asn Thr Pro Ala
325      330      335

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Ile Pro Ser Ser Lys Gly Asp Pro Phe Ile Gly Glu His Thr Glu Glu  
                   340                  345                  350  
 Ile Leu Glu Glu Phe Gly Phe Ser Arg Glu Glu Ile Tyr Gln Leu Asn  
                   355                  360                  365  
 Ser Asp Lys Ile Ile Glu Ser Asn Lys Val Lys Ala Ser Leu  
                   370                  375                  380

&lt;210&gt; 238

&lt;211&gt; 254

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 238  
 Met Asp Asn Tyr Ala Asp Leu Ser Asp Thr Glu Leu Thr Thr Leu Leu  
 1                  5                  10                  15  
 Arg Arg Tyr Asn Ile Pro His Gly Pro Val Val Gly Ser Thr Arg Arg  
                   20                  25                  30  
 Leu Tyr Glu Lys Lys Ile Phe Glu Tyr Glu Thr Gln Arg Arg Leu  
                   35                  40                  45  
 Ser Pro Pro Ser Ser Ser Ala Ala Ser Ser Tyr Ser Phe Ser Asp Leu  
                   50                  55                  60  
 Asn Ser Thr Arg Gly Asp Ala Asp Met Tyr Asp Leu Pro Lys Lys Glu  
 65                  70                  75                  80  
 Asp Ala Leu Leu Tyr Gln Ser Lys Gly Tyr Asn Asp Asp Tyr Tyr Glu  
                   85                  90                  95  
 Glu Ser Tyr Phe Thr Thr Arg Thr Tyr Gly Glu Pro Glu Ser Ala Gly  
                   100                  105                  110  
 Pro Ser Arg Ala Val Arg Gln Ser Val Thr Ser Phe Pro Asp Ala Asp  
                   115                  120                  125  
 Ala Phe His His Gln Val His Asp Asp Asp Leu Leu Ser Ser Ser Glu  
                   130                  135                  140  
 Glu Glu Cys Lys Asp Arg Glu Arg Pro Met Tyr Gly Arg Asp Ser Ala  
 145                  150                  155                  160  
 Tyr Gln Ser Ile Thr His Tyr Arg Pro Val Ser Ala Ser Arg Ser Ser  
                   165                  170                  175  
 Leu Asp Leu Ser Tyr Tyr Pro Thr Ser Ser Ser Thr Ser Phe Met Ser  
                   180                  185                  190  
 Ser Ser Ser Ser Ser Ser Trp Leu Thr Arg Arg Ala Ile Arg Pro  
                   195                  200                  205  
 Glu Asn Arg Ala Pro Gly Ala Gly Leu Gly Gln Asp Arg Gln Val Pro  
                   210                  215                  220  
 Leu Trp Gly Gln Leu Leu Leu Phe Leu Val Phe Val Ile Val Leu Phe  
 225                  230                  235                  240  
 Phe Ile Tyr His Phe Met Gln Ala Glu Glu Gly Asn Pro Phe  
                   245                  250

&lt;210&gt; 239

&lt;211&gt; 423

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 239  
 Met Ala Met Val Val Ser Ser Trp Arg Asp Pro Gln Asp Asp Val Ala  
 1 5 10 15  
 Gly Gly Asn Pro Gly Gly Pro Asn Pro Ala Ala Gln Ala Ala Arg Gly  
 20 25 30  
 Gly Gly Gly Gly Ala Gly Glu Gln Gln Gln Gln Ala Gly Ser Gly Ala  
 35 40 45  
 Pro His Thr Pro Gln Thr Pro Gly Gln Pro Gly Ala Pro Ala Thr Pro  
 50 55 60  
 Gly Thr Ala Gly Asp Lys Gly Gln Gly Pro Pro Gly Ser Gly Gln Ser  
 65 70 75 80  
 Gln Gln His Ile Glu Cys Val Val Cys Gly Asp Lys Ser Ser Gly Lys  
 85 90 95  
 His Tyr Gly Gln Phe Thr Cys Glu Gly Cys Lys Ser Phe Phe Lys Arg  
 100 105 110  
 Ser Val Arg Arg Asn Leu Thr Tyr Thr Cys Arg Ala Asn Arg Asn Cys  
 115 120 125  
 Pro Ile Asp Gln His His Arg Asn Gln Cys Gln Tyr Cys Arg Leu Lys  
 130 135 140  
 Lys Cys Leu Lys Val Gly Met Arg Arg Glu Ala Val Gln Arg Gly Arg  
 145 150 155 160  
 Met Pro Pro Thr Gln Pro Asn Pro Gly Gln Tyr Ala Leu Thr Asn Gly  
 165 170 175  
 Asp Pro Leu Asn Gly His Cys Tyr Leu Ser Gly Tyr Ile Ser Leu Leu  
 180 185 190  
 Leu Arg Ala Glu Pro Tyr Pro Thr Ser Arg Tyr Gly Ser Gln Cys Met  
 195 200 205  
 Gln Pro Asn Asn Ile Met Gly Ile Glu Asn Ile Cys Glu Leu Ala Ala  
 210 215 220  
 Arg Leu Leu Phe Ser Ala Val Glu Trp Ala Arg Asn Ile Pro Phe Phe  
 225 230 235 240  
 Pro Asp Leu Gln Ile Thr Asp Gln Val Ser Leu Leu Arg Leu Thr Trp  
 245 250 255  
 Ser Glu Leu Phe Val Leu Asn Ala Ala Gln Cys Ser Met Pro Leu His  
 260 265 270  
 Val Ala Pro Leu Leu Ala Ala Ala Gly Leu His Ala Ser Pro Met Ser  
 275 280 285  
 Ala Asp Arg Val Val Ala Phe Met Asp His Ile Arg Ile Phe Gln Glu  
 290 295 300  
 Gln Val Glu Lys Leu Lys Ala Leu His Val Asp Ser Ala Glu Tyr Ser  
 305 310 315 320  
 Cys Leu Lys Ala Ile Val Leu Phe Thr Ser Asp Ala Cys Gly Leu Ser  
 325 330 335  
 Asp Ala Ala His Ile Glu Ser Leu Gln Glu Lys Ser Gln Cys Ala Leu  
 340 345 350  
 Glu Glu Tyr Val Arg Ser Gln Tyr Pro Asn Gln Pro Ser Arg Phe Gly  
 355 360 365  
 Lys Leu Leu Leu Arg Leu Pro Ser Leu Arg Thr Val Ser Ser Ser Val  
 370 375 380  
 Ile Glu Gln Leu Phe Phe Val Arg Leu Val Gly Lys Thr Pro Ile Glu  
 385 390 395 400  
 Thr Leu Ile Arg Asp Met Leu Leu Ser Gly Ser Ser Phe Asn Trp Pro  
 405 410 415  
 Tyr Met Ser Ile Gln Cys Ser  
 420

&lt;210&gt; 240

&lt;211&gt; 536

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 240

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Met Lys Gln Ser Ser Asn Val Pro Ala Phe Leu Ser Lys Leu Trp Thr
1      5      10      15
Leu Val Glu Glu Thr His Thr Asn Glu Phe Ile Thr Trp Ser Gln Asn
20      25      30
Gly Gln Ser Phe Leu Val Leu Asp Glu Gln Arg Phe Ala Lys Glu Ile
35      40      45
Leu Pro Lys Tyr Phe Lys His Asn Asn Met Ala Ser Phe Val Arg Gln
50      55      60
Leu Asn Met Tyr Gly Phe Arg Lys Val Val His Ile Asp Ser Gly Ile
65      70      75      80
Val Lys Gln Glu Arg Asp Gly Pro Val Glu Phe Gln His Pro Tyr Phe
85      90      95
Lys Gln Gly Gln Asp Asp Leu Leu Glu Asn Ile Lys Arg Lys Val Ser
100      105      110
Ser Ser Lys Pro Glu Glu Asn Lys Ile Arg Gln Glu Asp Leu Thr Lys
115      120      125
Ile Ile Ser Ser Ala Gln Lys Val Gln Ile Lys Gln Glu Thr Ile Glu
130      135      140
Ser Arg Leu Ser Glu Leu Lys Ser Glu Asn Glu Ser Leu Trp Lys Glu
145      150      155      160
Val Ser Glu Leu Arg Ala Lys His Ala Gln Gln Gln Val Ile Arg
165      170      175
Lys Ile Val Gln Phe Ile Val Thr Leu Val Gln Asn Asn Gln Leu Val
180      185      190
Ser Leu Lys Arg Lys Arg Pro Leu Leu Leu Asn Thr Asn Gly Ala Gln
195      200      205
Lys Lys Asn Leu Phe Gln His Ile Val Lys Glu Pro Thr Asp Asn His
210      215      220
His His Lys Val Pro His Ser Arg Thr Glu Gly Leu Lys Pro Arg Glu
225      230      235      240
Arg Ile Ser Asp Asp Ile Ile Ile Tyr Asp Val Thr Asp Asp Asn Ala
245      250      255
Asp Glu Glu Asn Ile Pro Val Ile Pro Glu Thr Asn Glu Asp Val Ile
260      265      270
Ser Asp Pro Ser Asn Cys Ser Gln Tyr Pro Asp Ile Val Ile Val Glu
275      280      285
Asp Asp Asn Glu Asp Glu Tyr Ala Pro Val Ile Gln Ser Gly Glu Gln
290      295      300
Asn Glu Pro Ala Arg Glu Ser Leu Ser Ser Gly Ser Asp Gly Ser Ser
305      310      315      320
Pro Leu Met Ser Ser Ala Val Gln Leu Asn Gly Ser Ser Ser Leu Thr
325      330      335
Ser Glu Asp Pro Val Thr Met Met Asp Ser Ile Leu Asn Asp Asn Ile
340      345      350
Asn Leu Leu Gly Lys Val Glu Leu Leu Asp Tyr Leu Asp Ser Ile Asp
355      360      365
Cys Ser Leu Glu Asp Phe Gln Ala Met Leu Ser Gly Arg Gln Phe Ser
370      375      380
Ile Asp Pro Asp Leu Leu Val Asp Leu Phe Thr Ser Ser Val Gln Met
385      390      395      400

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Asn Pro Thr Asp Tyr Ile Asn Asn Thr Lys Ser Glu Asn Lys Gly Leu  
 405 410 415  
 Glu Thr Thr Lys Asn Asn Val Val Gln Pro Val Ser Glu Glu Gly Arg  
 420 425 430  
 Lys Ser Lys Ser Lys Pro Asp Lys Gln Leu Ile Gln Tyr Thr Ala Phe  
 435 440 445  
 Pro Leu Leu Ala Phe Leu Asp Gly Asn Pro Ala Ser Ser Val Glu Gln  
 450 455 460  
 Ala Ser Thr Thr Ala Ser Ser Glu Val Leu Ser Ser Val Asp Lys Pro  
 465 470 475 480  
 Ile Glu Val Asp Glu Leu Leu Asp Ser Ser Leu Asp Pro Glu Pro Thr  
 485 490 495  
 Gln Ser Lys Leu Val Arg Leu Glu Pro Leu Thr Glu Ala Glu Ala Ser  
 500 505 510  
 Glu Ala Thr Leu Phe Tyr Leu Cys Glu Leu Ala Pro Ala Pro Leu Asp  
 515 520 525  
 Ser Asp Met Pro Leu Leu Asp Ser  
 530 535

&lt;210&gt; 241

&lt;211&gt; 616

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 241

Met Asn Ser Pro Gly Gly Arg Gly Lys Lys Lys Gly Ser Gly Gly Ala  
 1 5 10 15  
 Ser Asn Pro Val Pro Pro Arg Pro Pro Pro Cys Leu Ala Pro Ala  
 20 25 30  
 Pro Pro Ala Ala Gly Pro Ala Pro Pro Pro Glu Ser Pro His Lys Arg  
 35 40 45  
 Asn Leu Tyr Tyr Phe Ser Tyr Pro Leu Phe Val Gly Phe Ala Leu Leu  
 50 55 60  
 Arg Leu Val Ala Phe His Leu Gly Leu Leu Phe Val Trp Leu Cys Gln  
 65 70 75 80  
 Arg Phe Ser Arg Ala Leu Met Ala Ala Lys Arg Ser Ser Gly Ala Ala  
 85 90 95  
 Pro Ala Pro Ala Ser Ala Ser Ala Pro Ala Pro Val Pro Gly Gly Glu  
 100 105 110  
 Ala Glu Arg Val Arg Val Phe His Lys Gln Ala Phe Glu Tyr Ile Ser  
 115 120 125  
 Ile Ala Leu Arg Ile Asp Glu Asp Glu Lys Ala Gly Gln Lys Glu Gln  
 130 135 140  
 Ala Val Glu Trp Tyr Lys Lys Gly Ile Glu Glu Leu Glu Lys Gly Ile  
 145 150 155 160  
 Ala Val Ile Val Thr Gly Gln Gly Glu Gln Cys Glu Arg Ala Arg Arg  
 165 170 175  
 Leu Gln Ala Lys Met Met Thr Asn Leu Val Met Ala Lys Asp Arg Leu  
 180 185 190  
 Gln Leu Leu Glu Lys Met Gln Pro Val Leu Pro Phe Ser Lys Ser Gln  
 195 200 205  
 Thr Asp Val Tyr Asn Asp Ser Thr Asn Leu Ala Cys Arg Asn Gly His  
 210 215 220  
 Leu Gln Ser Glu Ser Gly Ala Val Pro Lys Arg Lys Asp Pro Leu Thr  
 225 230 235 240  
 His Thr Ser Asn Ser Leu Pro Arg Ser Lys Thr Val Met Lys Thr Gly  
 245 250 255

Ser Ala Gly Leu Ser Gly His His Arg Ala Pro Ser Tyr Ser Gly Leu  
 260 265 270  
 Ser Met Val Ser Gly Val Lys Gln Gly Ser Gly Pro Ala Pro Thr Thr  
 275 280 285  
 His Lys Gly Thr Pro Lys Thr Asn Arg Thr Asn Lys Pro Ser Thr Pro  
 290 295 300  
 Thr Thr Ala Thr Arg Lys Lys Lys Asp Leu Lys Asn Phe Arg Asn Val  
 305 310 315 320  
 Asp Ser Asn Leu Ala Asn Leu Ile Met Asn Glu Ile Val Asp Asn Gly  
 325 330 335  
 Thr Ala Val Lys Phe Asp Asp Ile Ala Gly Gln Asp Leu Ala Lys Gln  
 340 345 350  
 Ala Leu Gln Glu Ile Val Ile Leu Pro Ser Leu Arg Pro Glu Leu Phe  
 355 360 365  
 Thr Gly Leu Arg Ala Pro Ala Arg Gly Leu Leu Leu Phe Gly Pro Pro  
 370 375 380  
 Gly Asn Gly Lys Thr Met Leu Ala Lys Ala Val Ala Ala Glu Ser Asn  
 385 390 395 400  
 Ala Thr Phe Phe Asn Ile Ser Ala Ala Ser Leu Thr Ser Lys Tyr Val  
 405 410 415  
 Gly Glu Gly Glu Lys Leu Val Arg Ala Leu Phe Ala Val Ala Arg Glu  
 420 425 430  
 Leu Gln Pro Ser Ile Ile Phe Ile Asp Glu Val Asp Ser Leu Leu Cys  
 435 440 445  
 Glu Arg Arg Glu Gly Glu His Asp Ala Ser Arg Arg Leu Lys Thr Glu  
 450 455 460  
 Phe Leu Ile Glu Phe Asp Gly Val Gln Ser Ala Gly Asp Asp Arg Val  
 465 470 475 480  
 Leu Val Met Gly Ala Thr Asn Arg Pro Gln Glu Leu Asp Glu Ala Val  
 485 490 495  
 Leu Arg Arg Phe Ile Lys Arg Val Tyr Val Ser Leu Pro Asn Glu Glu  
 500 505 510  
 Thr Arg Leu Leu Leu Lys Asn Leu Leu Cys Lys Gln Gly Ser Pro  
 515 520 525  
 Leu Thr Gln Lys Glu Leu Ala Gln Leu Ala Arg Met Thr Asp Gly Tyr  
 530 535 540  
 Ser Gly Ser Asp Leu Thr Ala Leu Ala Lys Asp Ala Ala Leu Gly Pro  
 545 550 555 560  
 Ile Arg Glu Leu Lys Pro Glu Gln Val Lys Asn Met Ser Ala Ser Glu  
 565 570 575  
 Met Arg Asn Ile Arg Leu Ser Asp Phe Thr Glu Ser Leu Lys Lys Ile  
 580 585 590  
 Lys Arg Ser Val Ser Pro Gln Thr Leu Glu Ala Tyr Ile Arg Trp Asn  
 595 600 605  
 Lys Asp Phe Gly Asp Thr Thr Val  
 610 615

&lt;210&gt; 242

&lt;211&gt; 1979

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 242

Met Ser Ser Trp Leu Gly Gly Leu Gly Ser Gly Leu Gly Gln Ser Leu  
 1 5 10 15  
 Gly Gln Val Gly Gly Ser Leu Ala Ser Leu Thr Gly Gln Ile Ser Asn  
 20 25 30

Phe Thr Lys Asp Met Leu Met Glu Gly Thr Glu Glu Val Glu Ala Glu  
 35 40 45  
 Leu Pro Asp Ser Arg Thr Lys Glu Ile Glu Ala Ile His Ala Ile Leu  
 50 55 60  
 Arg Ser Glu Asn Glu Arg Leu Lys Lys Leu Cys Thr Asp Leu Glu Glu  
 65 70 75 80  
 Lys His Glu Ala Ser Glu Ile Gln Ile Lys Gln Gln Ser Thr Ser Tyr  
 85 90 95  
 Arg Asn Gln Leu Gln Gln Lys Glu Val Glu Ile Ser His Leu Lys Ala  
 100 105 110  
 Arg Gln Ile Ala Leu Gln Asp Gln Leu Leu Lys Leu Gln Ser Ala Ala  
 115 120 125  
 Gln Ser Val Pro Ser Gly Ala Gly Val Pro Ala Thr Thr Ala Ser Ser  
 130 135 140  
 Ser Phe Ala Tyr Gly Ile Ser His His Pro Ser Ala Phe His Asp Asp  
 145 150 155 160  
 Asp Met Asp Phe Gly Asp Ile Ile Ser Ser Gln Gln Glu Ile Asn Arg  
 165 170 175  
 Leu Ser Asn Glu Val Ser Arg Leu Glu Ser Glu Val Gly His Trp Arg  
 180 185 190  
 His Ile Ala Gln Thr Ser Lys Ala Gln Gly Thr Asp Asn Ser Asp Gln  
 195 200 205  
 Ser Glu Ile Cys Lys Leu Gln Asn Ile Ile Lys Glu Leu Lys Gln Asn  
 210 215 220  
 Arg Ser Gln Glu Ile Asp Asp His Gln His Glu Met Ser Val Leu Gln  
 225 230 235 240  
 Asn Ala His Gln Gln Lys Leu Thr Glu Ile Ser Arg Arg His Arg Glu  
 245 250 255  
 Glu Leu Ser Asp Tyr Glu Glu Arg Ile Glu Glu Leu Glu Asn Leu Leu  
 260 265 270  
 Gln Gln Gly Gly Ser Gly Val Ile Glu Thr Asp Leu Ser Lys Ile Tyr  
 275 280 285  
 Glu Met Gln Lys Thr Ile Gln Val Leu Gln Ile Glu Lys Val Glu Ser  
 290 295 300  
 Thr Lys Lys Met Glu Gln Leu Glu Asp Lys Ile Lys Asp Ile Asn Lys  
 305 310 315 320  
 Lys Leu Ser Ser Ala Glu Asn Asp Arg Asp Ile Leu Arg Arg Glu Gln  
 325 330 335  
 Glu Gln Leu Asn Val Glu Lys Arg Gln Ile Met Glu Glu Cys Glu Asn  
 340 345 350  
 Leu Lys Leu Glu Cys Ser Lys Leu Gln Pro Ser Ala Val Lys Gln Ser  
 355 360 365  
 Asp Thr Met Thr Glu Lys Glu Arg Ile Leu Ala Gln Ser Ala Ser Val  
 370 375 380  
 Glu Glu Val Phe Arg Leu Gln Gln Ala Leu Ser Asp Ala Glu Asn Glu  
 385 390 395 400  
 Ile Met Arg Leu Ser Ser Leu Asn Gln Asp Asn Ser Leu Ala Glu Asp  
 405 410 415  
 Asn Leu Lys Leu Lys Met Arg Ile Glu Val Leu Glu Lys Glu Lys Ser  
 420 425 430  
 Leu Leu Ser Gln Glu Lys Glu Glu Leu Gln Met Ser Leu Leu Lys Leu  
 435 440 445  
 Asn Asn Glu Tyr Glu Val Ile Lys Ser Thr Ala Thr Arg Asp Ile Ser  
 450 455 460  
 Leu Asp Ser Glu Leu His Asp Leu Arg Leu Asn Leu Glu Ala Lys Glu  
 465 470 475 480  
 Gln Glu Leu Asn Gln Ser Ile Ser Glu Lys Glu Thr Leu Ile Ala Glu  
 485 490 495  
 Ile Glu Glu Leu Asp Arg Gln Asn Gln Glu Ala Thr Lys His Met Ile  
 500 505 510  
 Leu Ile Lys Asp Gln Leu Ser Lys Gln Gln Asn Glu Gly Asp Ser Ile  
 515 520 525

Ile Ser Lys Leu Lys Gln Asp Leu Asn Asp Glu Lys Lys Arg Val His  
 530 535 540  
 Gln Leu Glu Asp Asp Lys Met Asp Ile Thr Lys Glu Leu Asp Val Gln  
 545 550 555 560  
 Lys Glu Lys Leu Ile Gln Ser Glu Val Ala Leu Asn Asp Leu His Leu  
 565 570 575  
 Thr Lys Gln Lys Leu Glu Asp Lys Val Glu Asn Leu Val Asp Gln Leu  
 580 585 590  
 Asn Lys Ser Gln Glu Ser Asn Val Ser Ile Gln Lys Glu Asn Leu Glu  
 595 600 605  
 Leu Lys Glu His Ile Arg Gln Asn Glu Glu Glu Leu Ser Arg Ile Arg  
 610 615 620  
 Asn Glu Leu Met Gln Ser Leu Asn Gln Asp Ser Asn Ser Asn Phe Lys  
 625 630 635 640  
 Asp Thr Leu Leu Lys Glu Arg Glu Ala Glu Val Arg Asn Leu Lys Gln  
 645 650 655  
 Asn Leu Ser Glu Leu Glu Gln Leu Asn Glu Asn Leu Lys Lys Val Ala  
 660 665 670  
 Phe Asp Val Lys Met Glu Asn Glu Lys Leu Val Leu Ala Cys Glu Asp  
 675 680 685  
 Val Arg His Gln Leu Glu Glu Cys Leu Ala Gly Asn Asn Gln Leu Ser  
 690 695 700  
 Leu Glu Lys Asn Thr Ile Val Glu Thr Leu Lys Met Glu Lys Gly Glu  
 705 710 715 720  
 Ile Glu Ala Glu Leu Cys Trp Ala Lys Lys Arg Leu Leu Glu Glu Ala  
 725 730 735  
 Asn Lys Tyr Glu Lys Thr Ile Glu Glu Leu Ser Asn Ala Arg Asn Leu  
 740 745 750  
 Asn Thr Ser Ala Leu Gln Leu Glu His Glu His Leu Ile Lys Leu Asn  
 755 760 765  
 Gln Lys Lys Asp Met Glu Ile Ala Glu Leu Lys Lys Asn Ile Glu Gln  
 770 775 780  
 Met Asp Thr Asp His Lys Glu Thr Lys Asp Val Leu Ser Ser Ser Leu  
 785 790 795 800  
 Glu Glu Gln Lys Gln Leu Thr Gln Leu Ile Asn Lys Lys Glu Ile Phe  
 805 810 815  
 Ile Glu Lys Leu Lys Glu Arg Ser Ser Lys Leu Gln Glu Glu Asp  
 820 825 830  
 Lys Tyr Ser Gln Ala Leu Arg Lys Asn Glu Ile Leu Arg Gln Thr Ile  
 835 840 845  
 Glu Glu Lys Asp Arg Ser Leu Gly Ser Met Lys Glu Glu Asn Asn His  
 850 855 860  
 Leu Gln Glu Glu Leu Glu Arg Leu Arg Glu Glu Gln Ser Arg Thr Ala  
 865 870 875 880  
 Pro Val Ala Asp Pro Lys Thr Leu Asp Ser Val Thr Glu Leu Ala Ser  
 885 890 895  
 Glu Val Ser Gln Leu Asn Thr Ile Lys Glu His Leu Glu Glu Ile  
 900 905 910  
 Lys His His Gln Lys Ile Ile Glu Asp Gln Asn Gln Ser Lys Met Gln  
 915 920 925  
 Leu Leu Gln Ser Leu Gln Glu Gln Lys Lys Glu Met Asp Glu Phe Arg  
 930 935 940  
 Tyr Gln His Glu Gln Met Asn Ala Thr His Thr Gln Leu Phe Leu Glu  
 945 950 955 960  
 Lys Asp Glu Glu Ile Lys Ser Leu Gln Lys Thr Ile Glu Gln Ile Lys  
 965 970 975  
 Thr Gln Leu His Glu Glu Arg Gln Asp Ile Gln Thr Asp Asn Ser Asp  
 980 985 990  
 Ile Phe Gln Glu Thr Lys Val Gln Ser Leu Asn Ile Glu Asn Gly Ser  
 995 1000 1005  
 Glu Lys His Asp Leu Ser Lys Ala Glu Thr Glu Arg Leu Val Lys  
 1010 1015 1020



Gly Ile	Lys Glu Arg Glu Leu	Glu Ile Lys Leu Leu	Asn Glu Lys
1025	1030	1035	
Asn Ile	Ser Leu Thr Lys Gln	Ile Asp Gln Leu Ser	Lys Asp Glu
1040	1045	1050	
Val Gly	Lys Leu Thr Gln Ile	Ile Gln Gln Lys Asp	Leu Glu Ile
1055	1060	1065	
Gln Ala	Leu His Ala Arg Ile	Ser Ser Thr Ser His	Thr Gln Asp
1070	1075	1080	
Val Val	Tyr Leu Gln Gln Gln	Leu Gln Ala Tyr Ala	Met Glu Arg
1085	1090	1095	
Glu Lys	Val Phe Ala Val Leu	Asn Glu Lys Thr Arg	Glu Asn Ser
1100	1105	1110	
His Leu	Lys Thr Glu Tyr His	Lys Met Met Asp Ile	Val Ala Ala
1115	1120	1125	
Lys Glu	Ala Ala Leu Ile Lys	Leu Gln Asp Glu Asn	Lys Lys Leu
1130	1135	1140	
Ser Thr	Arg Phe Glu Ser Ser	Gly Gln Asp Met Phe	Arg Glu Thr
1145	1150	1155	
Ile Gln	Asn Leu Ser Arg Ile	Ile Arg Glu Lys Asp	Ile Glu Ile
1160	1165	1170	
Asp Ala	Leu Ser Gln Lys Cys	Gln Thr Leu Leu Ala	Val Leu Gln
1175	1180	1185	
Thr Ser	Ser Thr Gly Asn Glu	Ala Gly Gly Val Asn	Ser His Gln
1190	1195	1200	
Phe Glu	Glu Leu Leu Gln Glu	Arg Asp Lys Leu Lys	Gln Gln Val
1205	1210	1215	
Lys Lys	Met Glu Glu Trp Lys	Gln Gln Val Met Thr	Thr Val Gln
1220	1225	1230	
Asn Met	Gln His Glu Ser Ala	Gln Leu Gln Glu Glu	Leu His Gln
1235	1240	1245	
Leu Gln	Ala Gln Val Leu Val	Asp Ser Asp Asn Asn	Ser Lys Leu
1250	1255	1260	
Gln Val	Asp Tyr Thr Gly Leu	Ile Gln Ser Tyr Glu	Gln Asn Glu
1265	1270	1275	
Thr Lys	Leu Lys Asn Phe Gly	Gln Glu Leu Ala Gln	Val Gln His
1280	1285	1290	
Ser Ile	Gly Gln Leu Cys Asn	Thr Lys Asp Leu Leu	Leu Gly Lys
1295	1300	1305	
Leu Asp	Ile Ile Ser Pro Gln	Leu Ser Ser Ala Ser	Leu Leu Thr
1310	1315	1320	
Pro Gln	Ser Ala Glu Cys Leu	Arg Ala Ser Lys Ser	Glu Val Leu
1325	1330	1335	
Ser Glu	Ser Ser Glu Leu Leu	Gln Gln Glu Leu Glu	Glu Leu Arg
1340	1345	1350	
Lys Ser	Leu Gln Glu Lys Asp	Ala Thr Ile Arg Thr	Leu Gln Glu
1355	1360	1365	
Asn Asn	His Arg Leu Ser Asp	Ser Ile Ala Ala Thr	Ser Glu Leu
1370	1375	1380	
Glu Arg	Lys Glu His Glu Gln	Thr Asp Ser Glu Ile	Lys Gln Leu
1385	1390	1395	
Lys Glu	Lys Gln Asp Val Leu	Gln Lys Leu Leu Lys	Glu Lys Asp
1400	1405	1410	
Leu Leu	Ile Lys Ala Lys Ser	Asp Gln Leu Leu Ser	Ser Asn Glu
1415	1420	1425	
Asn Phe	Thr Asn Lys Val Asn	Glu Asn Glu Leu Leu	Arg Gln Ala
1430	1435	1440	
Val Thr	Asn Leu Lys Glu Arg	Ile Leu Ile Leu Glu	Met Asp Ile
1445	1450	1455	
Gly Lys	Leu Lys Gly Glu Asn	Glu Lys Ile Val Glu	Thr Tyr Arg
1460	1465	1470	
Gly Lys	Glu Thr Glu Tyr Gln	Ala Leu Gln Glu Thr	Asn Met Lys
1475	1480	1485	

Phe	Ser	Met	Met	Leu	Arg	Glu	Lys	Glu	Phe	Glu	Cys	His	Ser	Met
1490						1495					1500			
Lys	Glu	Lys	Ala	Leu	Ala	Phe	Glu	Gln	Leu	Leu	Lys	Glu	Lys	Glu
1505						1510					1515			
Gln	Gly	Lys	Thr	Gly	Glu	Leu	Asn	Gln	Leu	Leu	Asn	Ala	Val	Lys
1520						1525					1530			
Ser	Met	Gln	Glu	Lys	Thr	Val	Val	Phe	Gln	Gln	Glu	Arg	Asp	Gln
1535						1540					1545			
Val	Met	Leu	Ala	Leu	Lys	Gln	Lys	Gln	Met	Glu	Asn	Thr	Ala	Leu
1550						1555					1560			
Gln	Asn	Glu	Val	Gln	Arg	Leu	Arg	Asp	Lys	Glu	Phe	Arg	Ser	Asn
1565						1570					1575			
Gln	Glu	Leu	Glu	Arg	Leu	Arg	Asn	His	Leu	Leu	Glu	Ser	Glu	Asp
1580						1585					1590			
Ser	Tyr	Thr	Arg	Glu	Ala	Leu	Ala	Ala	Glu	Asp	Arg	Glu	Ala	Lys
1595						1600					1605			
Leu	Arg	Lys	Lys	Val	Thr	Val	Leu	Glu	Glu	Lys	Leu	Val	Ser	Ser
1610						1615					1620			
Ser	Asn	Ala	Met	Glu	Asn	Ala	Ser	His	Gln	Ala	Ser	Val	Gln	Val
1625						1630					1635			
Glu	Ser	Leu	Gln	Glu	Gln	Leu	Asn	Val	Val	Ser	Lys	Gln	Arg	Asp
1640						1645					1650			
Glu	Thr	Ala	Leu	Gln	Leu	Ser	Val	Ser	Gln	Glu	Gln	Val	Lys	Gln
1655						1660					1665			
Tyr	Ala	Leu	Ser	Leu	Ala	Asn	Leu	Gln	Met	Val	Leu	Glu	His	Phe
1670						1675					1680			
Gln	Gln	Glu	Glu	Lys	Ala	Met	Tyr	Ser	Ala	Glu	Leu	Glu	Lys	Gln
1685						1690					1695			
Lys	Gln	Leu	Ile	Ala	Glu	Trp	Lys	Lys	Asn	Ala	Glu	Asn	Leu	Glu
1700						1705					1710			
Gly	Lys	Val	Ile	Ser	Leu	Gln	Glu	Cys	Leu	Asp	Glu	Ala	Asn	Ala
1715						1720					1725			
Ala	Leu	Asp	Ser	Ala	Ser	Arg	Leu	Thr	Glu	Gln	Leu	Asp	Val	Lys
1730						1735					1740			
Glu	Glu	Gln	Ile	Glu	Glu	Leu	Lys	Arg	Gln	Asn	Glu	Leu	Arg	Gln
1745						1750					1755			
Glu	Met	Leu	Asp	Asp	Val	Gln	Lys	Lys	Leu	Met	Ser	Leu	Ala	Asn
1760						1765					1770			
Ser	Ser	Glu	Gly	Lys	Val	Asp	Lys	Val	Leu	Met	Arg	Asn	Leu	Phe
1775						1780					1785			
Ile	Gly	His	Phe	His	Thr	Pro	Lys	Asn	Gln	Arg	His	Glu	Val	Leu
1790						1795					1800			
Arg	Leu	Met	Gly	Ser	Ile	Leu	Gly	Val	Arg	Arg	Glu	Glu	Met	Glu
1805						1810					1815			
Gln	Leu	Phe	His	Asp	Asp	Gln	Gly	Ser	Val	Thr	Arg	Trp	Met	Thr
1820						1825					1830			
Gly	Trp	Leu	Gly	Gly	Gly	Ser	Lys	Ser	Val	Pro	Asn	Thr	Pro	Leu
1835						1840					1845			
Arg	Pro	Asn	Gln	Gln	Ser	Val	Val	Asn	Ser	Ser	Phe	Ser	Glu	Leu
1850						1855					1860			
Phe	Val	Lys	Phe	Leu	Glu	Thr	Glu	Ser	His	Pro	Ser	Ile	Pro	Pro
1865						1870					1875			
Pro	Lys	Leu	Ser	Val	His	Asp	Met	Lys	Pro	Leu	Asp	Ser	Pro	Gly
1880						1885					1890			
Arg	Arg	Lys	Arg	Asp	Thr	Asn	Ala	Pro	Glu	Ser	Phe	Lys	Asp	Thr
1895						1900					1905			
Ala	Glu	Ser	Arg	Ser	Gly	Arg	Arg	Thr	Asp	Val	Asn	Pro	Phe	Leu
1910						1915					1920			
Ala	Pro	Arg	Ser	Ala	Ala	Val	Pro	Leu	Ile	Asn	Pro	Ala	Gly	Leu
1925						1930					1935			
Gly	Pro	Gly	Gly	Pro	Gly	His	Leu	Leu	Leu	Lys	Pro	Ile	Ser	Asp
1940						1945					1950			

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Val Leu Pro Thr Phe Thr Pro Leu Pro Ala Leu Pro Asp Asn Ser  
 1955 1960 1965  
 Ala Gly Val Val Leu Lys Asp Leu Leu Lys Gln  
 1970 1975

&lt;210&gt; 243

&lt;211&gt; 522

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 243

Met Ser Ser Arg Pro Leu Glu Ser Pro Pro Pro Tyr Arg Pro Asp Glu  
 1 5 10 15  
 Phe Lys Pro Asn His Tyr Ala Pro Ser Asn Asp Ile Tyr Gly Gly Glu  
 20 25 30  
 Met His Val Arg Pro Met Leu Ser Gln Pro Ala Tyr Ser Phe Tyr Pro  
 35 40 45  
 Glu Asp Glu Ile Leu His Phe Tyr Lys Trp Thr Ser Pro Pro Gly Val  
 50 55 60  
 Ile Arg Ile Leu Ser Met Leu Ile Ile Val Met Cys Ile Ala Ile Phe  
 65 70 75 80  
 Ala Cys Val Ala Ser Thr Leu Ala Trp Asp Arg Gly Tyr Gly Thr Ser  
 85 90 95  
 Leu Leu Gly Gly Ser Val Gly Tyr Pro Tyr Gly Gly Ser Gly Phe Gly  
 100 105 110  
 Ser Tyr Gly Ser Gly Tyr Gly Tyr Gly Tyr Gly Tyr Gly Tyr  
 115 120 125  
 Gly Gly Tyr Thr Asp Pro Arg Ala Ala Lys Gly Phe Met Leu Ala Met  
 130 135 140  
 Ala Ala Phe Cys Phe Ile Ala Ala Leu Val Ile Phe Val Thr Ser Val  
 145 150 155 160  
 Ile Arg Ser Glu Met Ser Arg Thr Arg Arg Tyr Tyr Leu Ser Val Ile  
 165 170 175  
 Ile Val Ser Ala Ile Leu Gly Ile Met Val Phe Ile Ala Thr Ile Val  
 180 185 190  
 Tyr Ile Met Gly Val Asn Pro Thr Ala Gln Ser Ser Gly Ser Leu Tyr  
 195 200 205  
 Gly Ser Gln Ile Tyr Ala Leu Cys Asn Gln Phe Tyr Thr Pro Ala Ala  
 210 215 220  
 Thr Gly Leu Tyr Val Asp Gln Tyr Leu Tyr His Tyr Cys Val Val Asp  
 225 230 235 240  
 Pro Gln Glu Ala Ile Ala Ile Val Leu Gly Phe Met Ile Ile Val Ala  
 245 250 255  
 Phe Ala Leu Ile Phe Phe Ala Val Lys Thr Arg Arg Lys Met Asp  
 260 265 270  
 Arg Tyr Asp Lys Ser Asn Ile Leu Trp Asp Lys Glu His Ile Tyr Asp  
 275 280 285  
 Glu Gln Pro Pro Asn Val Glu Glu Trp Val Lys Asn Val Ser Ala Gly  
 290 295 300  
 Thr Gln Asp Val Pro Ser Pro Pro Ser Asp Tyr Val Glu Arg Val Asp  
 305 310 315 320  
 Ser Pro Met Ala Tyr Ser Ser Asn Gly Lys Val Asn Asp Lys Arg Phe  
 325 330 335  
 Tyr Pro Glu Ser Ser Tyr Lys Ser Thr Pro Val Pro Glu Val Val Gln  
 340 345 350  
 Glu Leu Pro Leu Thr Ser Pro Val Asp Asp Phe Arg Gln Pro Arg Tyr  
 355 360 365

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Ser Ser Gly Gly Asn Phe Glu Thr Pro Ser Lys Arg Ala Pro Ala Lys  
 370 375 380  
 Gly Arg Ala Gly Arg Ser Lys Arg Thr Glu Gln Asp His Tyr Glu Thr  
 385 390 395 400  
 Asp Tyr Thr Thr Gly Gly Glu Ser Cys Asp Glu Leu Glu Glu Asp Trp  
 405 410 415  
 Ile Arg Glu Tyr Pro Pro Ile Thr Ser Asp Gln Gln Arg Gln Leu Tyr  
 420 425 430  
 Lys Arg Asn Phe Asp Thr Gly Leu Gln Glu Tyr Lys Ser Leu Gln Ser  
 435 440 445  
 Glu Leu Asp Glu Ile Asn Lys Glu Leu Ser Arg Leu Asp Lys Glu Leu  
 450 455 460  
 Asp Asp Tyr Arg Glu Glu Ser Glu Glu Tyr Met Ala Ala Ala Asp Glu  
 465 470 475 480  
 Tyr Asn Arg Leu Lys Gln Val Lys Gly Ser Ala Asp Tyr Lys Ser Lys  
 485 490 495  
 Lys Asn His Cys Lys Gln Leu Lys Ser Lys Leu Ser His Ile Lys Lys  
 500 505 510  
 Met Val Gly Asp Tyr Asp Arg Gln Lys Thr  
 515 520

&lt;210&gt; 244

&lt;211&gt; 2181

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 244  
 Met Met Met Met Met Met Lys Lys Met Gln His Gln Arg Gln Gln  
 1 5 10 15  
 Gln Ala Asp His Ala Asn Glu Ala Asn Tyr Ala Arg Gly Thr Arg Leu  
 20 25 30  
 Pro Leu Ser Gly Glu Gly Pro Thr Ser Gln Pro Asn Ser Ser Lys Gln  
 35 40 45  
 Thr Val Leu Ser Trp Gln Ala Ile Asp Ala Ala Arg Gln Ala Lys  
 50 55 60  
 Ala Ala Gln Thr Met Ser Thr Ser Ala Pro Pro Pro Val Gly Ser Leu  
 65 70 75 80  
 Ser Gln Arg Lys Arg Gln Gln Tyr Ala Lys Ser Lys Lys Gln Gly Asn  
 85 90 95  
 Ser Ser Asn Ser Arg Pro Ala Arg Ala Leu Phe Cys Leu Ser Leu Asn  
 100 105 110  
 Asn Pro Ile Arg Arg Ala Cys Ile Ser Ile Val Glu Trp Lys Pro Phe  
 115 120 125  
 Asp Ile Phe Ile Leu Leu Ala Ile Phe Ala Asn Cys Val Ala Leu Ala  
 130 135 140  
 Ile Tyr Ile Pro Phe Pro Glu Asp Asp Ser Asn Ser Thr Asn His Asn  
 145 150 155 160  
 Leu Glu Lys Val Glu Tyr Ala Phe Leu Ile Ile Phe Thr Val Glu Thr  
 165 170 175  
 Phe Leu Lys Ile Ile Ala Tyr Gly Leu Leu Leu His Pro Asn Ala Tyr  
 180 185 190  
 Val Arg Asn Gly Trp Asn Leu Leu Asp Phe Val Ile Val Ile Val Gly  
 195 200 205  
 Leu Phe Ser Val Ile Leu Glu Gln Leu Thr Lys Glu Thr Glu Gly Gly  
 210 215 220  
 Asn His Ser Ser Gly Lys Ser Gly Gly Phe Asp Val Lys Ala Leu Arg  
 225 230 235 240

Ala Phe Arg Val Leu Arg Pro Leu Arg Leu Val Ser Gly Val Pro Ser  
 245 250 255  
 Leu Gln Val Val Leu Asn Ser Ile Ile Lys Ala Met Val Pro Leu Leu  
 260 265 270  
 His Ile Ala Leu Leu Val Leu Phe Val Ile Ile Ile Tyr Ala Ile Ile  
 275 280 285  
 Gly Leu Glu Leu Phe Ile Gly Lys Met His Lys Thr Cys Phe Phe Ala  
 290 295 300  
 Asp Ser Asp Ile Val Ala Glu Glu Asp Pro Ala Pro Cys Ala Phe Ser  
 305 310 315 320  
 Gly Asn Gly Arg Gln Cys Thr Ala Asn Gly Thr Glu Cys Arg Ser Gly  
 325 330 335  
 Trp Val Gly Pro Asn Gly Gly Ile Thr Asn Phe Asp Asn Phe Ala Phe  
 340 345 350  
 Ala Met Leu Thr Val Phe Gln Cys Ile Thr Met Glu Gly Trp Thr Asp  
 355 360 365  
 Val Leu Tyr Trp Val Asn Asp Ala Ile Gly Trp Glu Trp Pro Trp Val  
 370 375 380  
 Tyr Phe Val Ser Leu Ile Ile Leu Gly Ser Phe Phe Val Leu Asn Leu  
 385 390 395 400  
 Val Leu Gly Val Leu Ser Gly Glu Phe Ser Lys Glu Arg Glu Lys Ala  
 405 410 415  
 Lys Ala Arg Gly Asp Phe Gln Lys Leu Arg Glu Lys Gln Gln Leu Glu  
 420 425 430  
 Glu Asp Leu Lys Gly Tyr Leu Asp Trp Ile Thr Gln Ala Glu Asp Ile  
 435 440 445  
 Asp Pro Glu Asn Glu Glu Glu Gly Gly Glu Glu Gly Lys Arg Asn Thr  
 450 455 460  
 Ser Met Pro Thr Ser Glu Thr Glu Ser Val Asn Thr Glu Asn Val Ser  
 465 470 475 480  
 Gly Glu Gly Glu Asn Arg Gly Cys Cys Gly Ser Leu Trp Cys Trp Trp  
 485 490 495  
 Arg Arg Arg Gly Ala Ala Lys Ala Gly Pro Ser Gly Cys Arg Arg Trp  
 500 505 510  
 Gly Gln Ala Ile Ser Lys Ser Lys Leu Ser Arg Arg Trp Arg Arg Trp  
 515 520 525  
 Asn Arg Phe Asn Arg Arg Arg Cys Arg Ala Ala Val Lys Ser Val Thr  
 530 535 540  
 Phe Tyr Trp Leu Val Ile Val Leu Val Phe Leu Asn Thr Leu Thr Ile  
 545 550 555 560  
 Ser Ser Glu His Tyr Asn Gln Pro Asp Trp Leu Thr Gln Ile Gln Asp  
 565 570 575  
 Ile Ala Asn Lys Val Leu Leu Ala Leu Phe Thr Cys Glu Met Leu Val  
 580 585 590  
 Lys Met Tyr Ser Leu Gly Leu Gln Ala Tyr Phe Val Ser Leu Phe Asn  
 595 600 605  
 Arg Phe Asp Cys Phe Val Val Cys Gly Gly Ile Thr Glu Thr Ile Leu  
 610 615 620  
 Val Glu Leu Glu Ile Met Ser Pro Leu Gly Ile Ser Val Phe Arg Cys  
 625 630 635 640  
 Val Arg Leu Leu Arg Ile Phe Lys Val Thr Arg His Trp Thr Ser Leu  
 645 650 655  
 Ser Asn Leu Val Ala Ser Leu Leu Asn Ser Met Lys Ser Ile Ala Ser  
 660 665 670  
 Leu Leu Leu Leu Phe Leu Phe Ile Ile Ile Phe Ser Leu Leu Gly  
 675 680 685  
 Met Gln Leu Phe Gly Gly Lys Phe Asn Phe Asp Glu Thr Gln Thr Lys  
 690 695 700  
 Arg Ser Thr Phe Asp Asn Phe Pro Gln Ala Leu Leu Thr Val Phe Gln  
 705 710 715 720  
 Ile Leu Thr Gly Glu Asp Trp Asn Ala Val Met Tyr Asp Gly Ile Met  
 725 730 735

Ala Tyr Gly Gly Pro Ser Ser Ser Gly Met Ile Val Cys Ile Tyr Phe  
 740 745 750  
 Ile Ile Leu Phe Ile Cys Gly Asn Tyr Ile Leu Leu Asn Val Phe Leu  
 755 760 765  
 Ala Ile Ala Val Asp Asn Leu Ala Asp Ala Glu Ser Leu Asn Thr Ala  
 770 775 780  
 Gln Lys Glu Glu Ala Glu Glu Lys Glu Arg Lys Lys Ile Ala Arg Lys  
 785 790 795 800  
 Glu Ser Leu Glu Asn Lys Lys Asn Asn Lys Pro Glu Val Asn Gln Ile  
 805 810 815  
 Ala Asn Ser Asp Asn Lys Val Thr Ile Asp Asp Tyr Arg Glu Glu Asp  
 820 825 830  
 Glu Asp Lys Asp Pro Tyr Pro Pro Cys Asp Val Pro Val Gly Glu Glu  
 835 840 845  
 Glu Glu Glu Glu Glu Asp Glu Pro Glu Val Pro Ala Gly Pro Arg  
 850 855 860  
 Pro Arg Arg Ile Ser Glu Leu Asn Met Lys Glu Lys Ile Ala Pro Ile  
 865 870 875 880  
 Pro Glu Gly Ser Ala Phe Phe Ile Leu Ser Lys Thr Asn Pro Ile Arg  
 885 890 895  
 Val Gly Cys His Lys Leu Ile Asn His His Ile Phe Thr Asn Leu Ile  
 900 905 910  
 Leu Val Phe Ile Met Leu Ser Ser Ala Ala Leu Ala Ala Glu Asp Pro  
 915 920 925  
 Ile Arg Ser His Ser Phe Arg Asn Thr Ile Leu Gly Tyr Phe Asp Tyr  
 930 935 940  
 Ala Phe Thr Ala Ile Phe Thr Val Glu Ile Leu Lys Met Thr Thr  
 945 950 955 960  
 Phe Gly Ala Phe Leu His Lys Gly Ala Phe Cys Arg Asn Tyr Phe Asn  
 965 970 975 980  
 Leu Leu Asp Met Leu Val Val Gly Val Ser Leu Val Ser Phe Gly Ile  
 980 985 990  
 Gln Ser Ser Ala Ile Ser Val Val Lys Ile Leu Arg Val Leu Arg Val  
 995 1000 1005  
 Leu Arg Pro Leu Arg Ala Ile Asn Arg Ala Lys Gly Leu Lys His  
 1010 1015 1020  
 Val Val Gln Cys Val Phe Val Ala Ile Arg Thr Ile Gly Asn Ile  
 1025 1030 1035  
 Met Ile Val Thr Thr Leu Leu Gln Phe Met Phe Ala Cys Ile Gly  
 1040 1045 1050  
 Val Gln Leu Phe Lys Gly Lys Phe Tyr Arg Cys Thr Asp Glu Ala  
 1055 1060 1065  
 Lys Ser Asn Pro Glu Glu Cys Arg Gly Leu Phe Ile Leu Tyr Lys  
 1070 1075 1080  
 Asp Gly Asp Val Asp Ser Pro Val Val Arg Glu Arg Ile Trp Gln  
 1085 1090 1095  
 Asn Ser Asp Phe Asn Phe Asp Asn Val Leu Ser Ala Met Met Ala  
 1100 1105 1110  
 Leu Phe Thr Val Ser Thr Phe Glu Gly Trp Pro Ala Leu Leu Tyr  
 1115 1120 1125  
 Lys Ala Ile Asp Ser Asn Gly Glu Asn Ile Gly Pro Ile Tyr Asn  
 1130 1135 1140  
 His Arg Val Glu Ile Ser Ile Phe Phe Ile Ile Tyr Ile Ile Ile  
 1145 1150 1155  
 Val Ala Phe Phe Met Met Asn Ile Phe Val Gly Phe Val Ile Val  
 1160 1165 1170  
 Thr Phe Gln Glu Gln Gly Lys Glu Tyr Lys Asn Cys Glu Leu  
 1175 1180 1185  
 Asp Lys Asn Gln Arg Gln Cys Val Glu Tyr Ala Leu Lys Ala Arg  
 1190 1195 1200  
 Pro Leu Arg Arg Tyr Ile Pro Lys Asn Pro Tyr Gln Tyr Lys Phe  
 1205 1210 1215

Trp	Tyr	Val	Val	Asn	Ser	Ser	Pro	Phe	Glu	Tyr	Met	Met	Phe	Val
1220						1225					1230			
Leu	Ile	Met	Leu	Asn	Thr	Leu	Cys	Leu	Ala	Met	Gln	His	Tyr	Glu
1235						1240					1245			
Gln	Ser	Lys	Met	Phe	Asn	Asp	Ala	Met	Asp	Ile	Leu	Asn	Met	Val
1250						1255					1260			
Phe	Thr	Gly	Val	Phe	Thr	Val	Glu	Met	Val	Leu	Lys	Val	Ile	Ala
1265						1270					1275			
Phe	Lys	Pro	Lys	Gly	Tyr	Phe	Ser	Asp	Ala	Trp	Asn	Thr	Phe	Asp
1280						1285					1290			
Ser	Leu	Ile	Val	Ile	Gly	Ser	Ile	Ile	Asp	Val	Ala	Leu	Ser	Glu
1295						1300					1305			
Ala	Asp	Pro	Thr	Glu	Ser	Glu	Asn	Val	Pro	Val	Pro	Thr	Ala	Thr
1310						1315					1320			
Pro	Gly	Asn	Ser	Glu	Glu	Ser	Asn	Arg	Ile	Ser	Ile	Thr	Phe	Phe
1325						1330					1335			
Arg	Leu	Phe	Arg	Val	Met	Arg	Leu	Val	Lys	Leu	Leu	Ser	Arg	Gly
1340						1345					1350			
Glu	Gly	Ile	Arg	Thr	Leu	Leu	Trp	Thr	Phe	Ile	Lys	Ser	Phe	Gln
1355						1360					1365			
Ala	Leu	Pro	Tyr	Val	Ala	Leu	Leu	Ile	Ala	Met	Leu	Phe	Phe	Ile
1370						1375					1380			
Tyr	Ala	Val	Ile	Gly	Met	Gln	Met	Phe	Gly	Lys	Val	Ala	Met	Arg
1385						1390					1395			
Asp	Asn	Asn	Gln	Ile	Asn	Arg	Asn	Asn	Asn	Phe	Gln	Thr	Phe	Pro
1400						1405					1410			
Gln	Ala	Val	Leu	Leu	Leu	Phe	Arg	Cys	Ala	Thr	Gly	Glu	Ala	Trp
1415						1420					1425			
Gln	Glu	Ile	Met	Leu	Ala	Cys	Leu	Pro	Gly	Lys	Leu	Cys	Asp	Pro
1430						1435					1440			
Glu	Ser	Asp	Tyr	Asn	Pro	Gly	Glu	Glu	Tyr	Thr	Cys	Gly	Ser	Asn
1445						1450					1455			
Phe	Ala	Ile	Val	Tyr	Phe	Ile	Ser	Phe	Tyr	Met	Leu	Cys	Ala	Phe
1460						1465					1470			
Leu	Ile	Ile	Asn	Leu	Phe	Val	Ala	Val	Ile	Met	Asp	Asn	Phe	Asp
1475						1480					1485			
Tyr	Leu	Thr	Arg	Asp	Trp	Ser	Ile	Leu	Gly	Pro	His	His	Leu	Asp
1490						1495					1500			
Glu	Phe	Lys	Arg	Ile	Trp	Ser	Glu	Tyr	Asp	Pro	Glu	Ala	Lys	Gly
1505						1510					1515			
Arg	Ile	Lys	His	Leu	Asp	Val	Val	Thr	Leu	Leu	Arg	Arg	Ile	Gln
1520						1525					1530			
Pro	Pro	Leu	Gly	Phe	Gly	Lys	Leu	Cys	Pro	His	Arg	Val	Ala	Cys
1535						1540					1545			
Lys	Arg	Leu	Val	Ala	Met	Asn	Met	Pro	Leu	Asn	Ser	Asp	Gly	Thr
1550						1555					1560			
Val	Met	Phe	Asn	Ala	Thr	Leu	Phe	Ala	Leu	Val	Arg	Thr	Ala	Leu
1565						1570					1575			
Lys	Ile	Lys	Thr	Glu	Gly	Asn	Leu	Glu	Gln	Ala	Asn	Glu	Glu	Leu
1580						1585					1590			
Arg	Ala	Val	Ile	Lys	Lys	Ile	Trp	Lys	Lys	Thr	Ser	Met	Lys	Leu
1595						1600					1605			
Leu	Asp	Gln	Val	Val	Pro	Pro	Ala	Gly	Asp	Asp	Glu	Val	Thr	Val
1610						1615					1620			
Gly	Lys	Phe	Tyr	Ala	Thr	Phe	Leu	Ile	Gln	Asp	Tyr	Phe	Arg	Lys
1625						1630					1635			
Phe	Lys	Lys	Arg	Lys	Glu	Gln	Gly	Leu	Val	Gly	Lys	Tyr	Pro	Ala
1640						1645					1650			
Lys	Asn	Thr	Thr	Ile	Ala	Leu	Gln	Ala	Gly	Leu	Arg	Thr	Leu	His
1655						1660					1665			
Asp	Ile	Gly	Pro	Glu	Ile	Arg	Arg	Ala	Ile	Ser	Cys	Asp	Leu	Gln
1670						1675					1680			

Asp	Asp	Glu	Pro	Glu	Glu	Thr	Lys	Arg	Glu	Glu	Glu	Asp	Asp	Val
1685						1690					1695			
Phe	Lys	Arg	Asn	Gly	Ala	Leu	Leu	Gly	Asn	His	Val	Asn	His	Val
1700						1705					1710			
Asn	Ser	Asp	Arg	Arg	Asp	Ser	Leu	Gln	Gln	Thr	Asn	Thr	Thr	His
1715						1720					1725			
Arg	Pro	Leu	His	Val	Gln	Arg	Pro	Ser	Ile	Pro	Pro	Ala	Ser	Asp
1730						1735					1740			
Thr	Glu	Lys	Pro	Leu	Phe	Pro	Pro	Ala	Gly	Asn	Ser	Val	Cys	His
1745						1750					1755			
Asn	His	His	Asn	His	Asn	Ser	Ile	Gly	Lys	Gln	Val	Pro	Thr	Ser
1760						1765					1770			
Thr	Asn	Ala	Asn	Leu	Asn	Asn	Ala	Asn	Met	Ser	Lys	Ala	Ala	His
1775						1780					1785			
Gly	Lys	Arg	Pro	Ser	Ile	Gly	Asn	Leu	Glu	His	Val	Ser	Glu	Asn
1790						1795					1800			
Gly	His	His	Ser	Ser	His	Lys	His	Asp	Arg	Glu	Pro	Gln	Arg	Arg
1805						1810					1815			
Ser	Ser	Val	Lys	Arg	Thr	Arg	Tyr	Tyr	Glu	Thr	Tyr	Ile	Arg	Ser
1820						1825					1830			
Asp	Ser	Gly	Asp	Glu	Gln	Leu	Pro	Thr	Ile	Cys	Arg	Glu	Asp	Pro
1835						1840					1845			
Glu	Ile	His	Gly	Tyr	Phe	Arg	Asp	Pro	His	Cys	Leu	Gly	Glu	Gln
1850						1855					1860			
Glu	Tyr	Phe	Ser	Ser	Glu	Glu	Cys	Tyr	Glu	Asp	Asp	Ser	Ser	Pro
1865						1870					1875			
Thr	Trp	Ser	Arg	Gln	Asn	Tyr	Gly	Tyr	Tyr	Ser	Arg	Tyr	Pro	Gly
1880						1885					1890			
Arg	Asn	Ile	Asp	Ser	Glu	Arg	Pro	Arg	Gly	Tyr	His	His	Pro	Gln
1895						1900					1905			
Gly	Phe	Leu	Glu	Asp	Asp	Asp	Ser	Pro	Val	Cys	Tyr	Asp	Ser	Arg
1910						1915					1920			
Arg	Ser	Pro	Arg	Arg	Arg	Leu	Leu	Pro	Pro	Thr	Pro	Ala	Ser	His
1925						1930					1935			
Arg	Arg	Ser	Ser	Phe	Asn	Phe	Glu	Cys	Leu	Arg	Arg	Gln	Ser	Ser
1940						1945					1950			
Gln	Glu	Glu	Val	Pro	Ser	Ser	Pro	Ile	Phe	Pro	His	Arg	Thr	Ala
1955						1960					1965			
Leu	Pro	Leu	His	Leu	Met	Gln	Gln	Gln	Ile	Met	Ala	Val	Ala	Gly
1970						1975					1980			
Leu	Asp	Ser	Ser	Lys	Ala	Gln	Lys	Tyr	Ser	Pro	Ser	His	Ser	Thr
1985						1990					1995			
Arg	Ser	Trp	Ala	Thr	Pro	Pro	Ala	Thr	Pro	Pro	Tyr	Arg	Asp	Trp
2000						2005					2010			
Thr	Pro	Cys	Tyr	Thr	Pro	Leu	Ile	Gln	Val	Glu	Gln	Ser	Glu	Ala
2015						2020					2025			
Leu	Asp	Gln	Val	Asn	Gly	Ser	Leu	Pro	Ser	Leu	His	Arg	Ser	Ser
2030						2035					2040			
Trp	Tyr	Thr	Asp	Glu	Pro	Asp	Ile	Ser	Tyr	Arg	Thr	Phe	Thr	Pro
2045						2050					2055			
Ala	Ser	Leu	Thr	Val	Pro	Ser	Ser	Phe	Arg	Asn	Lys	Asn	Ser	Asp
2060						2065					2070			
Lys	Gln	Arg	Ser	Ala	Asp	Ser	Leu	Val	Glu	Ala	Val	Leu	Ile	Ser
2075						2080					2085			
Glu	Gly	Leu	Gly	Arg	Tyr	Ala	Arg	Asp	Pro	Lys	Phe	Val	Ser	Ala
2090						2095					2100			
Thr	Lys	His	Glu	Ile	Ala	Asp	Ala	Cys	Asp	Leu	Thr	Ile	Asp	Glu
2105						2110					2115			
Met	Glu	Ser	Ala	Ala	Ser	Thr	Leu	Leu	Asn	Gly	Asn	Val	Arg	Pro
2120						2125					2130			
Arg	Ala	Asn	Gly	Asp	Val	Gly	Pro	Leu	Ser	His	Arg	Gln	Asp	Tyr
2135						2140					2145			



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Glu Leu Gln Asp Phe Gly Pro Gly Tyr Ser Asp Glu Glu Pro Asp  
 2150 2155 2160  
 Pro Gly Arg Asp Glu Glu Asp Leu Ala Asp Glu Met Ile Cys Ile  
 2165 2170 2175  
 Thr Thr Leu  
 2180

&lt;210&gt; 245

&lt;211&gt; 377

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 245  
 Met Glu Leu Ser Val Leu Leu Phe Leu Ala Leu Leu Thr Gly Leu Leu  
 1 5 10 15  
 Leu Leu Leu Val Gln Arg His Pro Asn Ser His Gly Thr Leu Pro Pro  
 20 25 30  
 Gly Pro Arg Pro Leu Pro Leu Leu Gly Asn Leu Leu Gln Met Asp Arg  
 35 40 45  
 Arg Gly Leu Leu Lys Ser Phe Leu Arg Phe Arg Glu Lys Tyr Gly Asp  
 50 55 60  
 Val Phe Thr Val His Leu Gly Pro Arg Pro Val Val Met Leu Cys Gly  
 65 70 75 80  
 Val Glu Ala Ile Arg Glu Ala Leu Val Asp Asn Ala Glu Ala Phe Ser  
 85 90 95  
 Gly Arg Gly Lys Ile Val Ile Met Asp Pro Val Tyr Gln Gly Tyr Gly  
 100 105 110  
 Met Leu Phe Ala Asn Gly Asn Arg Trp Lys Val Leu Arg Arg Phe Ser  
 115 120 125  
 Val Thr Thr Met Arg Asp Phe Gly Met Gly Lys Arg Ser Val Glu Glu  
 130 135 140  
 Arg Ile Gln Asp Glu Ala Gln Cys Leu Ile Glu Glu Leu Arg Lys Ser  
 145 150 155 160  
 Lys Gly Ala Leu Val Asp Pro Thr Phe Leu Phe His Ser Ile Thr Ala  
 165 170 175  
 Asn Ile Ile Cys Ser Ile Ile Phe Gly Lys Arg Phe His Tyr Gln Asp  
 180 185 190  
 Gln Glu Phe Leu Lys Thr Leu Asn Leu Phe Cys Gln Ser Phe Leu Leu  
 195 200 205  
 Ile Ser Ser Ile Ser Ser Gln Leu Phe Glu Leu Phe Ser Gly Phe Leu  
 210 215 220  
 Lys Tyr Phe Pro Gly Ala His Arg Gln Val Tyr Lys Asn Leu Gln Glu  
 225 230 235 240  
 Ile Asn Ala Tyr Ile Gly His Ser Val Glu Lys His Arg Glu Thr Leu  
 245 250 255  
 Asp Pro Ser Ala Pro Arg Asp Leu Ile Asp Thr Tyr Leu Leu His Met  
 260 265 270  
 Glu Lys Glu Lys Ser Asn Pro His Ser Glu Phe Ser His Gln Asn Leu  
 275 280 285  
 Ile Ile Asn Thr Leu Ser Leu Phe Phe Ala Gly Thr Glu Thr Thr Ser  
 290 295 300  
 Thr Thr Leu Arg Tyr Gly Phe Leu Leu Met Leu Lys Tyr Pro His Val  
 305 310 315 320  
 Ala Glu Arg Val Tyr Lys Glu Ile Glu Gln Val Val Gly Pro His Arg  
 325 330 335  
 Pro Pro Ala Leu Asp Asp Arg Ala Lys Met Pro Tyr Thr Glu Ala Val  
 340 345 350

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Ile Arg Glu Ile Gln Arg Phe Ala Asp Leu Leu Pro Met Gly Val Pro  
           355                                  360                  365  
 His Ile Val Thr Gln His Thr Ser Phe  
       370                                  375

&lt;210&gt; 246

&lt;211&gt; 280

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 246

Met Ala Glu Lys Phe Asp Cys His Tyr Cys Arg Asp Pro Leu Gln Gly  
 1                  5                  10                  15  
 Lys Lys Tyr Val Gln Lys Asp Gly His His Cys Cys Leu Lys Cys Phe  
           20                  25                  30  
 Asp Lys Phe Cys Ala Asn Thr Cys Val Glu Cys Arg Lys Pro Ile Gly  
           35                  40                  45  
 Ala Asp Ser Lys Glu Val His Tyr Lys Asn Arg Phe Trp His Asp Thr  
           50                  55                  60  
 Cys Phe Arg Cys Ala Lys Cys Leu His Pro Leu Ala Asn Glu Thr Phe  
           65                  70                  75                  80  
 Val Ala Lys Asp Asn Lys Ile Leu Cys Asn Lys Cys Thr Thr Arg Glu  
           85                  90                  95  
 Asp Ser Pro Lys Cys Lys Gly Cys Phe Lys Ala Ile Val Ala Gly Asp  
           100                  105                  110  
 Gln Asn Val Glu Tyr Lys Gly Thr Val Trp His Lys Asp Cys Phe Thr  
           115                  120                  125  
 Cys Ser Asn Cys Lys Gln Val Ile Gly Thr Gly Ser Phe Phe Pro Lys  
           130                  135                  140  
 Gly Glu Asp Phe Tyr Cys Val Thr Cys His Glu Thr Lys Phe Ala Lys  
           145                  150                  155                  160  
 His Cys Val Lys Cys Asn Lys Ala Ile Thr Ser Gly Gly Ile Thr Tyr  
           165                  170                  175  
 Gln Asp Gln Pro Trp His Ala Asp Cys Phe Val Cys Val Thr Cys Ser  
           180                  185                  190  
 Lys Lys Leu Ala Gly Gln Arg Phe Thr Ala Val Glu Asp Gln Tyr Tyr  
           195                  200                  205  
 Cys Val Asp Cys Tyr Lys Asn Phe Val Ala Lys Lys Cys Ala Gly Cys  
           210                  215                  220  
 Lys Asn Pro Ile Thr Gly Phe Gly Lys Gly Ser Ser Val Val Ala Tyr  
           225                  230                  235                  240  
 Glu Gly Gln Ser Trp His Asp Tyr Cys Phe His Cys Lys Lys Cys Ser  
           245                  250                  255  
 Val Asn Leu Ala Asn Lys Arg Phe Val Phe His Gln Glu Gln Val Tyr  
           260                  265                  270  
 Cys Pro Asp Cys Ala Lys Lys Leu  
           275                  280

&lt;210&gt; 247

&lt;211&gt; 267

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 247  
 Met Ala Ser Pro Ser Lys Gly Asn Asp Leu Phe Ser Pro Asp Glu Glu  
 1 5 10 15  
 Gly Pro Ala Val Val Ala Gly Pro Gly Pro Gly Gly Ala Glu  
 20 25 30  
 Gly Ala Ala Glu Glu Arg Arg Val Lys Val Ser Ser Leu Pro Phe Ser  
 35 40 45  
 Val Glu Ala Leu Met Ser Asp Lys Lys Pro Pro Lys Glu Ala Ser Pro  
 50 55 60  
 Leu Pro Ala Glu Ser Ala Ser Ala Gly Ala Thr Leu Arg Pro Leu Leu  
 65 70 75 80  
 Leu Ser Gly His Gly Ala Arg Glu Ala His Ser Pro Gly Pro Leu Val  
 85 90 95  
 Lys Pro Phe Glu Thr Ala Ser Val Lys Ser Glu Asn Ser Glu Asp Gly  
 100 105 110  
 Ala Ala Trp Met Gln Glu Pro Gly Arg Tyr Ser Pro Pro Pro Arg His  
 115 120 125  
 Met Ser Pro Thr Thr Cys Thr Leu Arg Lys His Lys Thr Asn Arg Lys  
 130 135 140  
 Pro Arg Thr Pro Phe Thr Ser Gln Leu Leu Ala Leu Glu Arg Lys  
 145 150 155 160  
 Phe Arg Gln Lys Gln Tyr Leu Ser Ile Ala Glu Arg Ala Glu Phe Ser  
 165 170 175  
 Ser Ser Leu Asn Leu Thr Glu Thr Gln Val Lys Ile Trp Phe Gln Asn  
 180 185 190  
 Arg Arg Ala Lys Ala Lys Arg Leu Gln Glu Ala Glu Leu Glu Lys Leu  
 195 200 205  
 Lys Met Ala Ala Lys Pro Met Leu Pro Ser Ser Phe Ser Leu Pro Phe  
 210 215 220  
 Pro Ile Ser Ser Pro Leu Gln Ala Ala Ser Ile Tyr Gly Ala Ser Tyr  
 225 230 235 240  
 Pro Phe His Arg Pro Val Leu Pro Ile Pro Pro Val Gly Leu Tyr Ala  
 245 250 255  
 Thr Pro Val Gly Tyr Gly Met Tyr His Leu Ser  
 260 265

<210> 248

<211> 387

<212> PRT

<213> Homo sapiens

<400> 248  
 Met Pro Gly His Leu Gln Glu Gly Phe Gly Cys Val Val Thr Asn Arg  
 1 5 10 15  
 Phe Asp Gln Leu Phe Asp Asp Glu Ser Asp Pro Phe Glu Val Leu Lys  
 20 25 30  
 Ala Ala Glu Asn Lys Lys Lys Glu Ala Gly Gly Gly Val Gly Gly  
 35 40 45  
 Pro Gly Ala Lys Ser Ala Ala Gln Ala Ala Ala Gln Thr Asn Ser Asn  
 50 55 60  
 Ala Ala Gly Lys Gln Leu Arg Lys Glu Ser Gln Lys Asp Arg Lys Asn  
 65 70 75 80  
 Pro Leu Pro Pro Ser Val Gly Val Val Asp Lys Lys Glu Glu Thr Gln  
 85 90 95

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Pro Pro Val Ala Leu Lys Lys Glu Gly Ile Arg Arg Val Gly Arg Arg  
 100 105 110  
 Pro Asp Gln Gln Leu Gln Gly Glu Gly Lys Ile Ile Asp Arg Arg Pro  
 115 120 125  
 Glu Arg Arg Pro Pro Arg Glu Arg Arg Phe Glu Lys Pro Leu Glu Glu  
 130 135 140  
 Lys Gly Glu Gly Gly Glu Phe Ser Val Asp Arg Pro Ile Ile Asp Arg  
 145 150 155 160  
 Pro Ile Arg Gly Arg Gly Gly Leu Gly Arg Gly Arg Gly Gly Arg Gly  
 165 170 175  
 Arg Gly Met Gly Arg Gly Asp Gly Phe Asp Ser Arg Gly Lys Arg Glu  
 180 185 190  
 Phe Asp Arg His Ser Gly Ser Asp Arg Ser Gly Leu Lys His Glu Asp  
 195 200 205  
 Lys Arg Gly Gly Ser Gly Ser His Asn Trp Gly Thr Val Lys Asp Glu  
 210 215 220  
 Leu Thr Asp Leu Asp Gln Ser Asn Val Thr Glu Glu Thr Pro Glu Gly  
 225 230 235 240  
 Glu Glu His His Pro Val Ala Asp Thr Glu Asn Lys Glu Asn Glu Val  
 245 250 255  
 Glu Glu Val Lys Glu Glu Gly Pro Lys Glu Met Thr Leu Asp Glu Trp  
 260 265 270  
 Lys Ala Ile Gln Asn Lys Asp Arg Ala Lys Val Glu Phe Asn Ile Arg  
 275 280 285  
 Lys Pro Asn Glu Gly Ala Asp Gly Gln Trp Lys Lys Gly Phe Val Leu  
 290 295 300  
 His Lys Ser Lys Ser Glu Glu Ala His Ala Glu Asp Ser Val Met Asp  
 305 310 315 320  
 His His Phe Arg Lys Pro Ala Asn Asp Ile Thr Ser Gln Leu Glu Ile  
 325 330 335  
 Asn Phe Gly Asp Leu Gly Arg Pro Gly Arg Gly Gly Arg Gly Gly Arg  
 340 345 350  
 Gly Gly Arg Gly Arg Gly Gly Arg Pro Asn Arg Gly Ser Arg Thr Asp  
 355 360 365  
 Lys Ser Ser Ala Ser Ala Pro Asp Val Asp Asp Pro Glu Ala Phe Pro  
 370 375 380  
 Ala Leu Ala  
 385

&lt;210&gt; 249

&lt;211&gt; 239

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 249

Met Ala Ser Thr Ala Val Gln Leu Leu Gly Phe Leu Leu Ser Phe Leu  
 1 5 10 15  
 Gly Met Val Gly Thr Leu Ile Thr Thr Ile Leu Pro His Trp Arg Arg  
 20 25 30  
 Thr Ala His Val Gly Thr Asn Ile Leu Thr Ala Val Ser Tyr Leu Lys  
 35 40 45  
 Gly Leu Trp Met Glu Cys Val Trp His Ser Thr Gly Ile Tyr Gln Cys  
 50 55 60  
 Gln Ile Tyr Arg Ser Leu Leu Ala Leu Pro Gln Asp Leu Gln Ala Ala  
 65 70 75 80  
 Arg Ala Leu Met Val Ile Ser Cys Leu Leu Ser Gly Ile Ala Cys Ala  
 85 90 95

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Cys Ala Val Ile Gly Met Lys Cys Thr Arg Cys Ala Lys Gly Thr Pro  
 100 105 110  
 Ala Lys Thr Phe Ala Ile Leu Gly Gly Thr Leu Phe Ile Leu Ala  
 115 120 125  
 Gly Leu Leu Cys Met Val Ala Val Ser Trp Thr Thr Asn Asp Val Val  
 130 135 140  
 Gln Asn Phe Tyr Asn Pro Leu Leu Pro Ser Gly Met Lys Phe Glu Ile  
 145 150 155 160  
 Gly Gln Ala Leu Tyr Leu Gly Phe Ile Ser Ser Ser Leu Ser Leu Ile  
 165 170 175  
 Gly Gly Thr Leu Leu Cys Leu Ser Cys Gln Asp Glu Ala Pro Tyr Arg  
 180 185 190  
 Pro Tyr Gln Ala Pro Pro Arg Ala Thr Thr Thr Thr Ala Asn Thr Ala  
 195 200 205  
 Pro Ala Tyr Gln Pro Pro Ala Ala Tyr Lys Asp Asn Arg Ala Pro Ser  
 210 215 220  
 Val Thr Ser Ala Thr His Ser Gly Tyr Arg Leu Asn Asp Tyr Val  
 225 230 235

&lt;210&gt; 250

&lt;211&gt; 414

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 250  
 Met Gln Thr Phe Leu Lys Gly Lys Arg Val Gly Tyr Trp Leu Ser Glu  
 1 5 10 15  
 Lys Lys Ile Lys Lys Leu Asn Phe Gln Ala Phe Ala Glu Leu Cys Arg  
 20 25 30  
 Lys Arg Gly Met Glu Val Val Gln Leu Asn Leu Ser Arg Pro Ile Glu  
 35 40 45  
 Glu Gln Gly Pro Leu Asp Val Ile Ile His Lys Leu Thr Asp Val Ile  
 50 55 60  
 Leu Glu Ala Asp Gln Asn Asp Ser Gln Ser Leu Glu Leu Val His Arg  
 65 70 75 80  
 Phe Gln Glu Tyr Ile Asp Ala His Pro Glu Thr Ile Val Leu Asp Pro  
 85 90 95  
 Leu Pro Ala Ile Arg Thr Leu Leu Asp Arg Ser Lys Ser Tyr Glu Leu  
 100 105 110  
 Ile Arg Lys Ile Glu Ala Tyr Met Glu Asp Asp Arg Ile Cys Ser Pro  
 115 120 125  
 Pro Phe Met Glu Leu Thr Ser Leu Cys Gly Asp Asp Thr Met Arg Leu  
 130 135 140  
 Leu Glu Lys Asn Gly Leu Thr Phe Pro Phe Ile Cys Lys Thr Arg Val  
 145 150 155 160  
 Ala His Gly Thr Asn Ser His Glu Met Ala Ile Val Phe Asn Gln Glu  
 165 170 175  
 Gly Leu Asn Ala Ile Gln Pro Pro Cys Val Val Gln Asn Phe Ile Asn  
 180 185 190  
 His Asn Ala Val Leu Tyr Lys Val Phe Val Val Gly Glu Ser Tyr Thr  
 195 200 205  
 Val Val Gln Arg Pro Ser Leu Lys Asn Phe Ser Ala Gly Thr Ser Asp  
 210 215 220  
 Arg Glu Ser Ile Phe Phe Asn Ser His Asn Val Ser Lys Pro Glu Ser  
 225 230 235 240  
 Ser Ser Val Leu Thr Glu Leu Asp Lys Ile Glu Gly Val Phe Glu Arg  
 245 250 255

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Pro Ser Asp Glu Val Ile Arg Glu Leu Ser Arg Ala Leu Arg Gln Ala  
 260 265 270  
 Leu Gly Val Ser Leu Phe Gly Ile Asp Ile Ile Ile Asn Asn Gln Thr  
 275 280 285  
 Gly Gln His Ala Val Ile Asp Ile Asn Ala Phe Pro Gly Tyr Glu Gly  
 290 295 300  
 Val Ser Glu Phe Phe Thr Asp Leu Leu Asn His Ile Ala Thr Val Leu  
 305 310 315 320  
 Gln Gly Gln Ser Thr Ala Met Ala Ala Thr Gly Asp Val Ala Leu Leu  
 325 330 335  
 Arg His Ser Lys Leu Leu Ala Glu Pro Ala Gly Gly Leu Val Gly Glu  
 340 345 350  
 Arg Thr Cys Ser Ala Ser Pro Gly Cys Cys Gly Ser Met Met Gly Gln  
 355 360 365  
 Asp Ala Pro Trp Lys Ala Glu Ala Asp Ala Gly Gly Thr Ala Lys Leu  
 370 375 380  
 Pro His Gln Arg Leu Gly Cys Asn Ala Gly Val Ser Pro Ser Phe Gln  
 385 390 395 400  
 Gln His Cys Val Ala Ser Leu Ala Thr Lys Ala Ser Ser Gln  
 405 410

&lt;210&gt; 251

&lt;211&gt; 1255

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 251

Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu  
 1 5 10 15  
 Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys  
 20 25 30  
 Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His  
 35 40 45  
 Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr  
 50 55 60  
 Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val  
 65 70 75 80  
 Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu  
 85 90 95  
 Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr  
 100 105 110  
 Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro  
 115 120 125  
 Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser  
 130 135 140  
 Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln  
 145 150 155 160  
 Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn  
 165 170 175  
 Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys  
 180 185 190  
 His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser  
 195 200 205  
 Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys  
 210 215 220  
 Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys  
 225 230 235 240

Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu  
 245 250 255  
 His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val  
 260 265 270  
 Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg  
 275 280 285  
 Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu  
 290 295 300  
 Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln  
 305 310 315 320  
 Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys  
 325 330 335  
 Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu  
 340 345 350  
 Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys  
 355 360 365  
 Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp  
 370 375 380  
 Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe  
 385 390 395 400  
 Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro  
 405 410 415  
 Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg  
 420 425 430  
 Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu  
 435 440 445  
 Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly  
 450 455 460  
 Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val  
 465 470 475 480  
 Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr  
 485 490 495  
 Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His  
 500 505 510  
 Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys  
 515 520 525  
 Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys  
 530 535 540  
 Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys  
 545 550 555 560  
 Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys  
 565 570 575  
 Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp  
 580 585 590  
 Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu  
 595 600 605  
 Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln  
 610 615 620  
 Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys  
 625 630 635 640  
 Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Ile Val Ser  
 645 650 655  
 Ala Val Val Gly Ile Leu Leu Val Val Val Leu Gly Val Val Phe Gly  
 660 665 670  
 Ile Leu Ile Lys Arg Arg Gln Gln Lys Ile Arg Lys Tyr Thr Met Arg  
 675 680 685  
 Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly  
 690 695 700  
 Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu Leu  
 705 710 715 720  
 Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys  
 725 730 735

Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala Ile  
 740 745 750  
 Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile Leu  
 755 760 765  
 Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser Arg  
 770 775 780  
 Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln Leu  
 785 790 795 800  
 Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu Asn Arg Gly Arg  
 805 810 815  
 Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Met Gln Ile Ala Lys Gly  
 820 825 830  
 Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala Ala  
 835 840 845  
 Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe  
 850 855 860  
 Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala Asp  
 865 870 875 880  
 Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg  
 885 890 895  
 Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val  
 900 905 910  
 Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala  
 915 920 925  
 Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro  
 930 935 940  
 Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met  
 945 950 955 960  
 Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe  
 965 970 975  
 Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu  
 980 985 990  
 Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu  
 995 1000 1005  
 Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr  
 1010 1015 1020  
 Leu Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro Gly  
 1025 1030 1035  
 Ala Gly Gly Met Val His Arg His Arg Ser Ser Ser Thr Arg  
 1040 1045 1050  
 Ser Gly Gly Gly Asp Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu  
 1055 1060 1065  
 Glu Ala Pro Arg Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser  
 1070 1075 1080  
 Asp Val Phe Asp Gly Asp Leu Gly Met Gly Ala Ala Lys Gly Leu  
 1085 1090 1095  
 Gln Ser Leu Pro Thr His Asp Pro Ser Pro Leu Gln Arg Tyr Ser  
 1100 1105 1110  
 Glu Asp Pro Thr Val Pro Leu Pro Ser Glu Thr Asp Gly Tyr Val  
 1115 1120 1125  
 Ala Pro Leu Thr Cys Ser Pro Gln Pro Glu Tyr Val Asn Gln Pro  
 1130 1135 1140  
 Asp Val Arg Pro Gln Pro Pro Ser Pro Arg Glu Gly Pro Leu Pro  
 1145 1150 1155  
 Ala Ala Arg Pro Ala Gly Ala Thr Leu Glu Arg Ala Lys Thr Leu  
 1160 1165 1170  
 Ser Pro Gly Lys Asn Gly Val Val Lys Asp Val Phe Ala Phe Gly  
 1175 1180 1185  
 Gly Ala Val Glu Asn Pro Glu Tyr Leu Thr Pro Gln Gly Gly Ala  
 1190 1195 1200  
 Ala Pro Gln Pro His Pro Pro Pro Ala Phe Ser Pro Ala Phe Asp  
 1205 1210 1215



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Asn Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu Arg Gly Ala Pro  
 1220 1225 1230  
 Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn Pro Glu Tyr  
 1235 1240 1245  
 Leu Gly Leu Asp Val Pro Val  
 1250 1255

&lt;210&gt; 252

&lt;211&gt; 393

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 252

Met Glu Glu Pro Gln Ser Asp Pro Ser Val Glu Pro Pro Leu Ser Gln  
 1 5 10 15  
 Glu Thr Phe Ser Asp Leu Trp Lys Leu Leu Pro Glu Asn Asn Val Leu  
 20 25 30  
 Ser Pro Leu Pro Ser Gln Ala Met Asp Asp Leu Met Leu Ser Pro Asp  
 35 40 45  
 Asp Ile Glu Gln Trp Phe Thr Glu Asp Pro Gly Pro Asp Glu Ala Pro  
 50 55 60  
 Arg Met Pro Glu Ala Ala Pro Arg Val Ala Pro Ala Pro Ala Ala Pro  
 65 70 75 80  
 Thr Pro Ala Ala Pro Ala Pro Ala Pro Ser Trp Pro Leu Ser Ser Ser  
 85 90 95  
 Val Pro Ser Gln Lys Thr Tyr Gln Gly Ser Tyr Gly Phe Arg Leu Gly  
 100 105 110  
 Phe Leu His Ser Gly Thr Ala Lys Ser Val Thr Cys Thr Tyr Ser Pro  
 115 120 125  
 Ala Leu Asn Lys Met Phe Cys Gln Leu Ala Lys Thr Cys Pro Val Gln  
 130 135 140  
 Leu Trp Val Asp Ser Thr Pro Pro Pro Gly Thr Arg Val Arg Ala Met  
 145 150 155 160  
 Ala Ile Tyr Lys Gln Ser Gln His Met Thr Glu Val Val Arg Arg Cys  
 165 170 175  
 Pro His His Glu Arg Cys Ser Asp Ser Asp Gly Leu Ala Pro Pro Gln  
 180 185 190  
 His Leu Ile Arg Val Glu Gly Asn Leu Arg Val Glu Tyr Leu Asp Asp  
 195 200 205  
 Arg Asn Thr Phe Arg His Ser Val Val Val Pro Tyr Glu Pro Pro Glu  
 210 215 220  
 Val Gly Ser Asp Cys Thr Thr Ile His Tyr Asn Tyr Met Cys Asn Ser  
 225 230 235 240  
 Ser Cys Met Gly Gly Met Asn Arg Arg Pro Ile Leu Thr Ile Ile Thr  
 245 250 255  
 Leu Glu Asp Ser Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val  
 260 265 270  
 Arg Val Cys Ala Cys Pro Gly Arg Asp Arg Arg Thr Glu Glu Glu Asn  
 275 280 285  
 Leu Arg Lys Lys Gly Glu Pro His His Glu Leu Pro Pro Gly Ser Thr  
 290 295 300  
 Lys Arg Ala Leu Pro Asn Asn Thr Ser Ser Ser Pro Gln Pro Lys Lys  
 305 310 315 320  
 Lys Pro Leu Asp Gly Glu Tyr Phe Thr Leu Gln Ile Arg Gly Arg Glu  
 325 330 335  
 Arg Phe Glu Met Phe Arg Glu Leu Asn Glu Ala Leu Glu Leu Lys Asp  
 340 345 350

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Ala Gln Ala Gly Lys Glu Pro Gly Gly Ser Arg Ala His Ser Ser His  
 355 360 365  
 Leu Lys Ser Lys Lys Gly Gln Ser Thr Ser Arg His Lys Lys Leu Met  
 370 375 380  
 Phe Lys Thr Glu Gly Pro Asp Ser Asp  
 385 390

&lt;210&gt; 253

&lt;211&gt; 639

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 253

Met Ser Ala Arg Gly Pro Ala Ile Gly Ile Asp Leu Gly Thr Thr Tyr  
 1 5 10 15  
 Ser Cys Val Gly Val Phe Gln His Gly Lys Val Glu Ile Ile Ala Asn  
 20 25 30  
 Asp Gln Gly Asn Arg Thr Thr Pro Ser Tyr Val Ala Phe Thr Asp Thr  
 35 40 45  
 Glu Arg Leu Ile Gly Asp Ala Ala Lys Asn Gln Val Ala Met Asn Pro  
 50 55 60  
 Thr Asn Thr Ile Phe Asp Ala Lys Arg Leu Ile Gly Arg Lys Phe Glu  
 65 70 75 80  
 Asp Ala Thr Val Gln Ser Asp Met Lys His Trp Pro Phe Arg Val Val  
 85 90 95  
 Ser Glu Gly Gly Lys Pro Lys Val Gln Val Glu Tyr Lys Gly Glu Thr  
 100 105 110  
 Lys Thr Phe Phe Pro Glu Glu Ile Ser Ser Met Val Leu Thr Lys Met  
 115 120 125  
 Lys Glu Ile Ala Glu Ala Tyr Leu Gly Gly Lys Val His Ser Ala Val  
 130 135 140  
 Ile Thr Val Pro Ala Tyr Phe Asn Asp Ser Gln Arg Gln Ala Thr Lys  
 145 150 155 160  
 Asp Ala Gly Thr Ile Thr Gly Leu Asn Val Leu Arg Ile Ile Asn Glu  
 165 170 175  
 Pro Thr Ala Ala Ala Ile Ala Tyr Gly Leu Asp Lys Lys Gly Cys Ala  
 180 185 190  
 Gly Gly Glu Lys Asn Val Leu Ile Phe Asp Leu Gly Gly Gly Thr Phe  
 195 200 205  
 Asp Val Ser Ile Leu Thr Ile Glu Asp Gly Ile Phe Glu Val Lys Ser  
 210 215 220  
 Thr Ala Gly Asp Thr His Leu Gly Gly Glu Asp Phe Asp Asn Arg Met  
 225 230 235 240  
 Val Ser His Leu Ala Glu Glu Phe Lys Arg Lys His Lys Lys Asp Ile  
 245 250 255  
 Gly Pro Asn Lys Arg Ala Val Arg Arg Leu Arg Thr Ala Cys Glu Arg  
 260 265 270  
 Ala Lys Arg Thr Leu Ser Ser Ser Thr Gln Ala Ser Ile Glu Ile Asp  
 275 280 285  
 Ser Leu Tyr Glu Gly Val Asp Phe Tyr Thr Ser Ile Thr Arg Ala Arg  
 290 295 300  
 Phe Glu Glu Leu Asn Ala Asp Leu Phe Arg Gly Thr Leu Glu Pro Val  
 305 310 315 320  
 Glu Lys Ala Leu Arg Asp Ala Lys Leu Asp Lys Gly Gln Ile Gln Glu  
 325 330 335  
 Ile Val Leu Val Gly Gly Ser Thr Arg Ile Pro Lys Ile Gln Lys Leu  
 340 345 350

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Leu Gln Asp Phe Phe Asn Gly Lys Glu Leu Asn Lys Ser Ile Asn Pro  
 355 360 365  
 Asp Glu Ala Val Ala Tyr Gly Ala Ala Val Gln Ala Ala Ile Leu Ile  
 370 375 380  
 Gly Asp Lys Ser Glu Asn Val Gln Asp Leu Leu Leu Asp Val Thr  
 385 390 395 400  
 Pro Leu Ser Leu Gly Ile Glu Thr Ala Gly Gly Val Met Thr Pro Leu  
 405 410 415  
 Ile Lys Arg Asn Thr Thr Ile Pro Thr Lys Gln Thr Gln Thr Phe Thr  
 420 425 430  
 Thr Tyr Ser Asp Asn Gln Ser Ser Val Leu Val Gln Val Tyr Glu Gly  
 435 440 445  
 Glu Arg Ala Met Thr Lys Asp Asn Asn Leu Leu Gly Lys Phe Asp Leu  
 450 455 460  
 Thr Gly Ile Pro Pro Ala Pro Arg Gly Val Pro Gln Ile Glu Val Thr  
 465 470 475 480  
 Phe Asp Ile Asp Ala Asn Gly Ile Leu Asn Val Thr Ala Ala Asp Lys  
 485 490 495  
 Ser Thr Gly Lys Glu Asn Lys Ile Thr Ile Thr Asn Asp Lys Gly Arg  
 500 505 510  
 Leu Ser Lys Asp Asp Ile Asp Arg Met Val Gln Glu Ala Glu Arg Tyr  
 515 520 525  
 Lys Ser Glu Asp Glu Ala Asn Arg Asp Arg Val Ala Lys Asn Ala  
 530 535 540  
 Leu Glu Ser Tyr Thr Tyr Asn Ile Lys Gln Thr Val Glu Asp Glu Lys  
 545 550 555 560  
 Leu Arg Gly Lys Ile Ser Glu Gln Asp Lys Asn Lys Ile Leu Asp Lys  
 565 570 575  
 Cys Gln Glu Val Ile Asn Trp Leu Asp Arg Asn Gln Met Ala Glu Lys  
 580 585 590  
 Asp Glu Tyr Glu His Lys Gln Lys Glu Leu Glu Arg Val Cys Asn Pro  
 595 600 605  
 Ile Ile Ser Lys Leu Tyr Gln Gly Gly Pro Gly Gly Ser Gly Gly  
 610 615 620  
 Gly Gly Ser Gly Ala Ser Gly Gly Pro Thr Ile Glu Glu Val Asp  
 625 630 635

&lt;210&gt; 254

&lt;211&gt; 1094

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 254

Met Ala Arg Pro Val Arg Gly Gly Leu Gly Ala Pro Arg Arg Ser Pro  
 1 5 10 15  
 Cys Leu Leu Leu Leu Trp Leu Leu Leu Arg Leu Glu Pro Val Thr  
 20 25 30  
 Ala Ala Ala Gly Pro Arg Ala Pro Cys Ala Ala Ala Cys Thr Cys Ala  
 35 40 45  
 Gly Asp Ser Leu Asp Cys Gly Gly Arg Gly Leu Ala Ala Leu Pro Gly  
 50 55 60  
 Asp Leu Pro Ser Trp Thr Arg Ser Leu Asn Leu Ser Tyr Asn Lys Leu  
 65 70 75 80  
 Ser Glu Ile Asp Pro Ala Gly Phe Glu Asp Leu Pro Asn Leu Gln Glu  
 85 90 95  
 Val Tyr Leu Asn Asn Glu Leu Thr Ala Val Pro Ser Leu Gly Ala  
 100 105 110

Ala	Ser	Ser	His	Val	Val	Ser	Leu	Phe	Leu	Gln	His	Asn	Lys	Ile	Arg	
		115					120					125				
Ser	Val	Glu	Gly	Ser	Gln	Leu	Lys	Ala	Tyr	Leu	Ser	Leu	Glu	Val	Leu	
		130				135					140					
Asp	Leu	Ser	Leu	Asn	Asn	Ile	Thr	Glu	Val	Arg	Asn	Thr	Cys	Phe	Pro	
145				150						155					160	
His	Gly	Pro	Pro	Ile	Lys	Glu	Leu	Asn	Leu	Ala	Gly	Asn	Arg	Ile	Gly	
				165						170				175		
Thr	Leu	Glu	Leu	Gly	Ala	Phe	Asp	Gly	Leu	Ser	Arg	Ser	Leu	Leu	Thr	
			180					185					190			
Leu	Arg	Leu	Ser	Lys	Asn	Arg	Ile	Thr	Gln	Leu	Pro	Val	Arg	Ala	Phe	
		195					200					205				
Lys	Leu	Pro	Arg	Leu	Thr	Gln	Leu	Asp	Leu	Asn	Arg	Asn	Arg	Ile	Arg	
		210				215					220					
Leu	Ile	Glu	Gly	Leu	Thr	Phe	Gln	Gly	Leu	Asn	Ser	Leu	Glu	Val	Leu	
225				230						235					240	
Lys	Leu	Gln	Arg	Asn	Asn	Ile	Ser	Lys	Leu	Thr	Asp	Gly	Ala	Phe	Trp	
				245					250					255		
Gly	Leu	Ser	Lys	Met	His	Val	Leu	His	Leu	Glu	Tyr	Asn	Ser	Leu	Val	
			260					265					270			
Glu	Val	Asn	Ser	Gly	Ser	Leu	Tyr	Gly	Leu	Thr	Ala	Leu	His	Gln	Leu	
		275					280					285				
His	Leu	Ser	Asn	Asn	Ser	Ile	Ala	Arg	Ile	His	Arg	Lys	Gly	Trp	Ser	
		290				295					300					
Phe	Cys	Gln	Lys	Leu	His	Glu	Leu	Val	Leu	Ser	Phe	Asn	Asn	Leu	Thr	
305				310						315					320	
Arg	Leu	Asp	Glu	Glu	Ser	Leu	Ala	Glu	Leu	Ser	Ser	Leu	Ser	Val	Leu	
				325					330					335		
Arg	Leu	Ser	His	Asn	Ser	Ile	Ser	His	Ile	Ala	Glu	Gly	Ala	Phe	Lys	
			340					345					350			
Gly	Leu	Arg	Ser	Leu	Arg	Val	Leu	Asp	Leu	Asp	His	Asn	Glu	Ile	Ser	
		355					360					365				
Gly	Thr	Ile	Glu	Asp	Thr	Ser	Gly	Ala	Phe	Ser	Gly	Leu	Asp	Ser	Leu	
		370				375					380					
Ser	Lys	Leu	Thr	Leu	Phe	Gly	Asn	Lys	Ile	Lys	Ser	Val	Ala	Lys	Arg	
385				390						395					400	
Ala	Phe	Ser	Gly	Leu	Glu	Gly	Leu	Glu	His	Leu	Asn	Leu	Gly	Gly	Asn	
				405					410					415		
Ala	Ile	Arg	Ser	Val	Gln	Phe	Asp	Ala	Phe	Val	Lys	Met	Lys	Asn	Leu	
			420					425					430			
Lys	Glu	Leu	His	Ile	Ser	Ser	Asp	Ser	Phe	Leu	Cys	Asp	Cys	Gln	Leu	
		435					440					445				
Lys	Trp	Leu	Pro	Pro	Trp	Leu	Ile	Gly	Arg	Met	Leu	Gln	Ala	Phe	Val	
		450				455					460					
Thr	Ala	Thr	Cys	Ala	His	Pro	Glu	Ser	Leu	Lys	Gly	Gln	Ser	Ile	Phe	
465				470						475					480	
Ser	Val	Pro	Pro	Glu	Ser	Phe	Val	Cys	Asp	Asp	Phe	Leu	Lys	Pro	Gln	
				485					490					495		
Ile	Ile	Thr	Gln	Pro	Glu	Thr	Thr	Met	Ala	Met	Val	Gly	Lys	Asp	Ile	
			500					505					510			
Arg	Phe	Thr	Cys	Ser	Ala	Ala	Ser	Ser	Ser	Ser	Ser	Pro	Met	Thr	Phe	
		515					520					525				
Ala	Trp	Lys	Lys	Asp	Asn	Glu	Val	Leu	Thr	Asn	Ala	Asp	Met	Glu	Asn	
		530				535					540					
Phe	Val	His	Val	His	Ala	Gln	Asp	Gly	Glu	Val	Met	Glu	Tyr	Thr	Thr	
545				550						555					560	
Ile	Leu	His	Leu	Arg	Gln	Val	Thr	Phe	Gly	His	Glu	Gly	Arg	Tyr	Gln	
				565					570					575		
Cys	Val	Ile	Thr	Asn	His	Phe	Gly	Ser	Thr	Tyr	Ser	His	Lys	Ala	Arg	
			580					585					590			
Leu	Thr	Val	Asn	Val	Leu	Pro	Ser	Phe	Thr	Lys	Thr	Pro	His	Asp	Ile	
		595					600						605			

Thr Ile Arg Thr Thr Thr Met Ala Arg Leu Glu Cys Ala Ala Thr Gly  
 610 615 620  
 His Pro Asn Pro Gln Ile Ala Trp Gln Lys Asp Gly Gly Thr Asp Phe  
 625 630 635 640  
 Pro Ala Ala Arg Glu Arg Arg Met His Val Met Pro Asp Asp Asp Val  
 645 650 655  
 Phe Phe Ile Thr Asp Val Lys Ile Asp Asp Ala Gly Val Tyr Ser Cys  
 660 665 670  
 Thr Ala Gln Asn Ser Ala Gly Ser Ile Ser Ala Asn Ala Thr Leu Thr  
 675 680 685  
 Val Leu Glu Thr Pro Ser Leu Val Val Pro Leu Glu Asp Arg Val Val  
 690 695 700  
 Ser Val Gly Glu Thr Val Ala Leu Gln Cys Lys Ala Thr Gly Asn Pro  
 705 710 715 720  
 Pro Pro Arg Ile Thr Trp Phe Lys Gly Asp Arg Pro Leu Ser Leu Thr  
 725 730 735  
 Glu Arg His His Leu Thr Pro Asp Asn Gln Leu Leu Val Val Gln Asn  
 740 745 750  
 Val Val Ala Glu Asp Ala Gly Arg Tyr Thr Cys Glu Met Ser Asn Thr  
 755 760 765  
 Leu Gly Thr Glu Arg Ala His Ser Gln Leu Ser Val Leu Pro Ala Ala  
 770 775 780  
 Gly Cys Arg Lys Asp Gly Thr Thr Val Gly Ile Phe Thr Ile Ala Val  
 785 790 795 800  
 Val Ser Ser Ile Val Leu Thr Ser Leu Val Trp Val Cys Ile Ile Tyr  
 805 810 815  
 Gln Thr Arg Lys Lys Ser Glu Glu Tyr Ser Val Thr Asn Thr Asp Glu  
 820 825 830  
 Thr Val Val Pro Pro Asp Val Pro Ser Tyr Leu Ser Ser Gln Gly Thr  
 835 840 845  
 Leu Ser Asp Arg Gln Glu Thr Val Val Arg Thr Glu Gly Ala Gly Pro  
 850 855 860  
 Gln Ala Asn Gly His Ile Glu Ser Asn Gly Val Cys Pro Arg Asp Ala  
 865 870 875 880  
 Ser His Phe Pro Glu Pro Asp Thr His Ser Val Ala Cys Arg Gln Pro  
 885 890 895  
 Lys Leu Cys Ala Gly Ser Ala Tyr His Lys Glu Pro Trp Lys Ala Ile  
 900 905 910  
 Glu Lys Ala Glu Gly Thr Pro Gly Pro His Lys Met Glu His Gly Gly  
 915 920 925  
 Arg Val Val Cys Ser Asp Cys Asn Thr Glu Val Asp Cys Tyr Ser Arg  
 930 935 940  
 Gly Gln Ala Phe His Pro Gln Pro Val Ser Arg Asp Ser Ala Gln Pro  
 945 950 955 960  
 Ser Ala Pro Asn Gly Pro Glu Pro Gly Gly Ser Asp Gln Glu His Ser  
 965 970 975  
 Pro His His Gln Cys Ser Arg Thr Ala Ala Gly Ser Cys Pro Glu Cys  
 980 985 990  
 Gln Gly Ser Leu Tyr Pro Ser Asn His Asp Arg Met Leu Thr Ala Val  
 995 1000 1005  
 Lys Lys Lys Pro Met Ala Ser Leu Asp Gly Lys Gly Asp Ser Ser  
 1010 1015 1020  
 Trp Thr Leu Ala Arg Leu Tyr His Pro Asp Ser Thr Glu Leu Gln  
 1025 1030 1035  
 Pro Ala Ser Ser Leu Thr Ser Gly Ser Pro Glu Arg Ala Glu Ala  
 1040 1045 1050  
 Gln Tyr Leu Leu Val Ser Asn Gly His Leu Pro Lys Ala Cys Asp  
 1055 1060 1065  
 Ala Ser Pro Glu Ser Thr Pro Leu Thr Gly Gln Leu Pro Gly Lys  
 1070 1075 1080  
 Gln Arg Val Pro Leu Leu Leu Ala Pro Lys Ser  
 1085 1090

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&lt;210&gt; 255

&lt;211&gt; 474

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

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<400> 255
Met Ala Thr Asn Trp Gly Ser Leu Leu Gln Asp Lys Gln Gln Leu Glu
1      5      10      15
Glu Leu Ala Arg Gln Ala Val Asp Arg Ala Leu Ala Glu Gly Val Leu
      20      25      30
Leu Arg Thr Ser Gln Glu Pro Thr Ser Ser Glu Val Val Ser Tyr Ala
      35      40      45
Pro Phe Thr Leu Phe Pro Ser Leu Val Pro Ser Ala Leu Leu Glu Gln
      50      55      60
Ala Tyr Ala Val Gln Met Asp Phe Asn Leu Leu Val Asp Ala Val Ser
65      70      75      80
Gln Asn Ala Ala Phe Leu Glu Gln Thr Leu Ser Ser Thr Ile Lys Gln
      85      90      95
Asp Asp Phe Thr Ala Arg Leu Phe Asp Ile His Lys Gln Val Leu Lys
      100      105      110
Glu Gly Ile Ala Gln Thr Val Phe Leu Gly Leu Asn Arg Ser Asp Tyr
      115      120      125
Met Phe Gln Arg Ser Ala Asp Gly Ser Pro Ala Leu Lys Gln Ile Glu
      130      135      140
Ile Asn Thr Ile Ser Ala Ser Phe Gly Gly Leu Ala Ser Arg Thr Pro
145      150      155      160
Ala Val His Arg His Val Leu Ser Val Leu Ser Lys Thr Lys Glu Ala
      165      170      175
Gly Lys Ile Leu Ser Asn Asn Pro Ser Lys Gly Leu Ala Leu Gly Ile
      180      185      190
Ala Lys Ala Trp Glu Leu Tyr Gly Ser Pro Asn Ala Leu Val Leu Leu
      195      200      205
Ile Ala Gln Glu Lys Glu Arg Asn Ile Phe Asp Gln Arg Ala Ile Glu
210      215      220
Asn Glu Leu Leu Ala Arg Asn Ile His Val Ile Arg Arg Thr Phe Glu
225      230      235      240
Asp Ile Ser Glu Lys Gly Ser Leu Asp Gln Asp Arg Arg Leu Phe Val
      245      250      255
Asp Gly Gln Glu Ile Ala Val Val Tyr Phe Arg Asp Gly Tyr Met Pro
      260      265      270
Arg Gln Tyr Ser Leu Gln Asn Trp Glu Ala Arg Leu Leu Leu Glu Arg
      275      280      285
Ser His Ala Ala Lys Cys Pro Asp Ile Ala Thr Gln Leu Ala Gly Thr
290      295      300
Lys Lys Val Gln Gln Glu Leu Ser Arg Pro Gly Met Leu Glu Met Leu
305      310      315      320
Leu Pro Gly Gln Pro Glu Ala Val Ala Arg Leu Arg Ala Thr Phe Ala
      325      330      335
Gly Leu Tyr Ser Leu Asp Val Gly Glu Glu Gly Asp Gln Ala Ile Ala
      340      345      350
Glu Ala Leu Ala Ala Pro Ser Arg Phe Val Leu Lys Pro Gln Arg Glu
      355      360      365
Gly Gly Gly Asn Asn Leu Tyr Gly Glu Glu Met Val Gln Ala Leu Lys
370      375      380
Gln Leu Lys Asp Ser Glu Glu Arg Ala Ser Tyr Ile Leu Met Glu Lys
385      390      395      400

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Ile Glu Pro Glu Pro Phe Glu Asn Cys Leu Leu Arg Pro Gly Ser Pro  
 405 410 415  
 Ala Arg Val Val Gln Cys Ile Ser Glu Leu Gly Ile Phe Gly Val Tyr  
 420 425 430  
 Val Arg Gln Glu Lys Thr Leu Val Met Asn Lys His Val Gly His Leu  
 435 440 445  
 Leu Arg Thr Lys Ala Ile Glu His Ala Asp Gly Gly Val Ala Ala Gly  
 450 455 460  
 Val Ala Val Leu Asp Asn Pro Tyr Pro Val  
 465 470

&lt;210&gt; 256

&lt;211&gt; 96

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 256  
 Met Trp Ile Tyr Ser Lys Leu Ser Lys Arg Thr Val Phe Arg Lys Gly  
 1 5 10 15  
 Lys Thr Arg Thr Gln Lys Thr Leu Gly Ile Thr Thr Thr Pro Lys Cys  
 20 25 30  
 Phe Arg Leu Gln Glu Ile Thr Ile His Val Phe Ala Gly Gly His Thr  
 35 40 45  
 Ile Phe Pro Tyr Tyr Leu Val Gln Asn Asp Ser Ser Leu Pro Lys Ser  
 50 55 60  
 Phe Phe Ser Asn His Asp Phe Pro Ile Tyr Phe Gly Pro Met Gln Ser  
 65 70 75 80  
 His Ser Leu Trp Pro Ile Val Ser Leu Pro Thr Thr Pro Leu Gly Gly  
 85 90 95

&lt;210&gt; 257

&lt;211&gt; 3256

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 257  
 Met Trp Pro Thr Arg Arg Leu Val Thr Ile Lys Arg Ser Gly Val Asp  
 1 5 10 15  
 Gly Pro His Phe Pro Leu Ser Leu Ser Thr Cys Leu Phe Gly Arg Gly  
 20 25 30  
 Ile Glu Cys Asp Ile Arg Ile Gln Leu Pro Val Val Ser Lys Gln His  
 35 40 45  
 Cys Lys Ile Glu Ile His Glu Gln Glu Ala Ile Leu His Asn Phe Ser  
 50 55 60  
 Ser Thr Asn Pro Thr Gln Val Asn Gly Ser Val Ile Asp Glu Pro Val  
 65 70 75 80  
 Arg Leu Lys His Gly Asp Val Ile Thr Ile Asp Arg Ser Phe Arg  
 85 90 95  
 Tyr Glu Asn Glu Ser Leu Gln Asn Gly Arg Lys Ser Thr Glu Phe Pro  
 100 105 110  
 Arg Lys Ile Arg Glu Gln Glu Pro Ala Arg Arg Val Ser Arg Ser Ser  
 115 120 125

Phe	Ser	Ser	Asp	Pro	Asp	Glu	Lys	Ala	Gln	Asp	Ser	Lys	Ala	Tyr	Ser
130						135					140				
Lys	Ile	Thr	Glu	Gly	Lys	Val	Ser	Gly	Asn	Pro	Gln	Val	His	Ile	Lys
145					150					155					160
Asn	Val	Lys	Glu	Asp	Ser	Thr	Ala	Asp	Asp	Ser	Lys	Asp	Ser	Val	Ala
				165					170						175
Gln	Gly	Thr	Thr	Asn	Val	His	Ser	Ser	Glu	His	Ala	Gly	Arg	Asn	Gly
			180					185					190		
Arg	Asn	Ala	Ala	Asp	Pro	Ile	Ser	Gly	Asp	Phe	Lys	Glu	Ile	Ser	Ser
			195				200					205			
Val	Lys	Leu	Val	Ser	Arg	Tyr	Gly	Glu	Leu	Lys	Ser	Val	Pro	Thr	Thr
			210			215					220				
Gln	Cys	Leu	Asp	Asn	Ser	Lys	Lys	Asn	Glu	Ser	Pro	Phe	Trp	Lys	Leu
225					230					235					240
Tyr	Glu	Ser	Val	Lys	Lys	Glu	Leu	Asp	Val	Lys	Ser	Gln	Lys	Glu	Asn
				245					250					255	
Val	Leu	Gln	Tyr	Cys	Arg	Lys	Ser	Gly	Leu	Gln	Thr	Asp	Tyr	Ala	Thr
			260					265					270		
Glu	Lys	Glu	Ser	Ala	Asp	Gly	Leu	Gln	Gly	Glu	Thr	Gln	Leu	Leu	Val
			275				280					285			
Ser	Arg	Lys	Ser	Arg	Pro	Lys	Ser	Gly	Gly	Ser	Gly	His	Ala	Val	Ala
			290			295					300				
Glu	Pro	Ala	Ser	Pro	Glu	Gln	Glu	Leu	Asp	Gln	Asn	Lys	Gly	Lys	Gly
305					310					315					320
Arg	Asp	Val	Glu	Ser	Val	Gln	Thr	Pro	Ser	Lys	Ala	Val	Gly	Ala	Ser
				325					330					335	
Phe	Pro	Leu	Tyr	Glu	Pro	Ala	Lys	Met	Lys	Thr	Pro	Val	Gln	Tyr	Ser
			340					345						350	
Gln	Gln	Gln	Asn	Ser	Pro	Gln	Lys	His	Lys	Asn	Lys	Asp	Leu	Tyr	Thr
			355				360					365			
Thr	Gly	Arg	Arg	Glu	Ser	Val	Asn	Leu	Gly	Lys	Ser	Glu	Gly	Phe	Lys
			370			375					380				
Ala	Gly	Asp	Lys	Thr	Leu	Thr	Pro	Arg	Lys	Leu	Ser	Thr	Arg	Asn	Arg
385					390					395					400
Thr	Pro	Ala	Lys	Val	Glu	Asp	Ala	Ala	Asp	Ser	Ala	Thr	Lys	Pro	Glu
				405					410					415	
Asn	Leu	Ser	Ser	Lys	Thr	Arg	Gly	Ser	Ile	Pro	Thr	Asp	Val	Glu	Val
			420					425					430		
Leu	Pro	Thr	Glu	Thr	Glu	Ile	His	Asn	Glu	Pro	Phe	Leu	Thr	Leu	Trp
			435				440					445			
Leu	Thr	Gln	Val	Glu	Arg	Lys	Ile	Gln	Lys	Asp	Ser	Leu	Ser	Lys	Pro
			450			455					460				
Glu	Lys	Leu	Gly	Thr	Thr	Ala	Gly	Gln	Met	Cys	Ser	Gly	Leu	Pro	Gly
465					470					475					480
Leu	Ser	Ser	Val	Asp	Ile	Asn	Asn	Phe	Gly	Asp	Ser	Ile	Asn	Glu	Ser
				485					490					495	
Glu	Gly	Ile	Pro	Leu	Lys	Arg	Arg	Arg	Val	Ser	Phe	Gly	Gly	His	Leu
			500					505					510		
Arg	Pro	Glu	Leu	Phe	Asp	Glu	Asn	Leu	Pro	Pro	Asn	Thr	Pro	Leu	Lys
			515				520						525		
Arg	Gly	Glu	Ala	Pro	Thr	Lys	Arg	Lys	Ser	Leu	Val	Met	His	Thr	Pro
			530			535					540				
Pro	Val	Leu	Lys	Lys	Ile	Ile	Lys	Glu	Gln	Pro	Gln	Pro	Ser	Gly	Lys
545					550					555					560
Gln	Glu	Ser	Gly	Ser	Glu	Ile	His	Val	Glu	Val	Lys	Ala	Gln	Ser	Leu
				565					570					575	
Val	Ile	Ser	Pro	Pro	Ala	Pro	Ser	Pro	Arg	Lys	Thr	Pro	Val	Ala	Ser
			580					585					590		
Asp	Gln	Arg	Arg	Arg	Ser	Cys	Lys	Thr	Ala	Pro	Ala	Ser	Ser	Ser	Lys
			595				600					605			
Ser	Gln	Thr	Glu	Val	Pro	Lys	Arg	Gly	Gly	Glu	Arg	Val	Ala	Thr	Cys
			610			615					620				



Leu Gln Lys Arg Val Ser Ile Ser Arg Ser Gln His Asp Ile Leu Gln  
 625 630 635 640  
 Met Ile Cys Ser Lys Arg Arg Ser Gly Ala Ser Glu Ala Asn Leu Ile  
 645 650 655  
 Val Ala Lys Ser Trp Ala Asp Val Val Lys Leu Gly Ala Lys Gln Thr  
 660 665 670  
 Gln Thr Lys Val Ile Lys His Gly Pro Gln Arg Ser Met Asn Lys Arg  
 675 680 685  
 Gln Arg Arg Pro Ala Thr Pro Lys Lys Pro Val Gly Glu Val His Ser  
 690 700  
 Gln Phe Ser Thr Gly His Ala Asn Ser Pro Cys Thr Ile Ile Ile Gly  
 705 710 715 720  
 Lys Ala His Thr Glu Lys Val His Val Pro Ala Arg Pro Tyr Arg Val  
 725 730 735  
 Leu Asn Asn Phe Ile Ser Asn Gln Lys Met Asp Phe Lys Glu Asp Leu  
 740 745 750  
 Ser Gly Ile Ala Glu Met Phe Lys Thr Pro Val Lys Glu Gln Pro Gln  
 755 760 765  
 Leu Thr Ser Thr Cys His Ile Ala Ile Ser Asn Ser Glu Asn Leu Leu  
 770 775 780  
 Gly Lys Gln Phe Gln Gly Thr Asp Ser Gly Glu Glu Pro Leu Leu Pro  
 785 790 795 800  
 Thr Ser Glu Ser Phe Gly Gly Asn Val Phe Phe Ser Ala Gln Asn Ala  
 805 810 815  
 Ala Lys Gln Pro Ser Asp Lys Cys Ser Ala Ser Pro Pro Leu Arg Arg  
 820 825 830  
 Gln Cys Ile Arg Glu Asn Gly Asn Val Ala Lys Thr Pro Arg Asn Thr  
 835 840 845  
 Tyr Lys Met Thr Ser Leu Glu Thr Lys Thr Ser Asp Thr Glu Thr Glu  
 850 855 860  
 Pro Ser Lys Thr Val Ser Thr Val Asn Arg Ser Gly Arg Ser Thr Glu  
 865 870 875 880  
 Phe Arg Asn Ile Gln Lys Leu Pro Val Glu Ser Lys Ser Glu Glu Thr  
 885 890 895  
 Asn Thr Glu Ile Val Glu Cys Ile Leu Lys Arg Gly Gln Lys Ala Thr  
 900 905 910  
 Leu Leu Gln Gln Arg Arg Glu Gly Glu Met Lys Glu Ile Glu Arg Pro  
 915 920 925  
 Phe Glu Thr Tyr Lys Glu Asn Ile Glu Leu Lys Glu Asn Asp Glu Lys  
 930 935 940  
 Met Lys Ala Met Lys Arg Ser Arg Thr Trp Gly Gln Lys Cys Ala Pro  
 945 950 955 960  
 Met Ser Asp Leu Thr Asp Leu Lys Ser Leu Pro Asp Thr Glu Leu Met  
 965 970 975  
 Lys Asp Thr Ala Arg Gly Gln Asn Leu Leu Gln Thr Gln Asp His Ala  
 980 985 990  
 Lys Ala Pro Lys Ser Glu Lys Gly Lys Ile Thr Lys Met Pro Cys Gln  
 995 1000 1005  
 Ser Leu Gln Pro Glu Pro Ile Asn Thr Pro Thr His Thr Lys Gln  
 1010 1015 1020  
 Gln Leu Lys Ala Ser Leu Gly Lys Val Gly Val Lys Glu Glu Leu  
 1025 1030 1035  
 Leu Ala Val Gly Lys Phe Thr Arg Thr Ser Gly Glu Thr Thr His  
 1040 1045 1050  
 Thr His Arg Glu Pro Ala Gly Asp Gly Lys Ser Ile Arg Thr Phe  
 1055 1060 1065  
 Lys Glu Ser Pro Lys Gln Ile Leu Asp Pro Ala Ala Arg Val Thr  
 1070 1075 1080  
 Gly Met Lys Lys Trp Pro Arg Thr Pro Lys Glu Glu Ala Gln Ser  
 1085 1090 1095  
 Leu Glu Asp Leu Ala Gly Phe Lys Glu Leu Phe Gln Thr Pro Gly  
 1100 1105 1110

Pro	Ser	Glu	Glu	Ser	Met	Thr	Asp	Glu	Lys	Thr	Thr	Lys	Ile	Ala
1115						1120						1125		
Cys	Lys	Ser	Pro	Pro	Pro	Glu	Ser	Val	Asp	Thr	Pro	Thr	Ser	Thr
1130						1135						1140		
Lys	Gln	Trp	Pro	Lys	Arg	Ser	Leu	Arg	Lys	Ala	Asp	Val	Glu	Glu
1145						1150						1155		
Glu	Phe	Leu	Ala	Leu	Arg	Lys	Leu	Thr	Pro	Ser	Ala	Gly	Lys	Ala
1160						1165						1170		
Met	Leu	Thr	Pro	Lys	Pro	Ala	Gly	Gly	Asp	Glu	Lys	Asp	Ile	Lys
1175						1180						1185		
Ala	Phe	Met	Gly	Thr	Pro	Val	Gln	Lys	Leu	Asp	Leu	Ala	Gly	Thr
1190						1195						1200		
Leu	Pro	Gly	Ser	Lys	Arg	Gln	Leu	Gln	Thr	Pro	Lys	Glu	Lys	Ala
1205						1210						1215		
Gln	Ala	Leu	Glu	Asp	Leu	Ala	Gly	Phe	Lys	Glu	Leu	Phe	Gln	Thr
1220						1225						1230		
Pro	Gly	His	Thr	Glu	Glu	Leu	Val	Ala	Ala	Gly	Lys	Thr	Thr	Lys
1235						1240						1245		
Ile	Pro	Cys	Asp	Ser	Pro	Gln	Ser	Asp	Pro	Val	Asp	Thr	Pro	Thr
1250						1255						1260		
Ser	Thr	Lys	Gln	Arg	Pro	Lys	Arg	Ser	Ile	Arg	Lys	Ala	Asp	Val
1265						1270						1275		
Glu	Gly	Glu	Leu	Leu	Ala	Cys	Arg	Asn	Leu	Met	Pro	Ser	Ala	Gly
1280						1285						1290		
Lys	Ala	Met	His	Thr	Pro	Lys	Pro	Ser	Val	Gly	Glu	Glu	Lys	Asp
1295						1300						1305		
Ile	Ile	Ile	Phe	Val	Gly	Thr	Pro	Val	Gln	Lys	Leu	Asp	Leu	Thr
1310						1315						1320		
Glu	Asn	Leu	Thr	Gly	Ser	Lys	Arg	Arg	Pro	Gln	Thr	Pro	Lys	Glu
1325						1330						1335		
Glu	Ala	Gln	Ala	Leu	Glu	Asp	Leu	Thr	Gly	Phe	Lys	Glu	Leu	Phe
1340						1345						1350		
Gln	Thr	Pro	Gly	His	Thr	Glu	Glu	Ala	Val	Ala	Ala	Gly	Lys	Thr
1355						1360						1365		
Thr	Lys	Met	Pro	Cys	Glu	Ser	Ser	Pro	Pro	Glu	Ser	Ala	Asp	Thr
1370						1375						1380		
Pro	Thr	Ser	Thr	Arg	Arg	Gln	Pro	Lys	Thr	Pro	Leu	Glu	Lys	Arg
1385						1390						1395		
Asp	Val	Gln	Lys	Glu	Leu	Ser	Ala	Leu	Lys	Lys	Leu	Thr	Gln	Thr
1400						1405						1410		
Ser	Gly	Glu	Thr	Thr	His	Thr	Asp	Lys	Val	Pro	Gly	Gly	Glu	Asp
1415						1420						1425		
Lys	Ser	Ile	Asn	Ala	Phe	Arg	Glu	Thr	Ala	Lys	Gln	Lys	Leu	Asp
1430						1435						1440		
Pro	Ala	Ala	Ser	Val	Thr	Gly	Ser	Lys	Arg	His	Pro	Lys	Thr	Lys
1445						1450						1455		
Glu	Lys	Ala	Gln	Pro	Leu	Glu	Asp	Leu	Ala	Gly	Trp	Lys	Glu	Leu
1460						1465						1470		
Phe	Gln	Thr	Pro	Val	Cys	Thr	Asp	Lys	Pro	Thr	Thr	His	Glu	Lys
1475						1480						1485		
Thr	Thr	Lys	Ile	Ala	Cys	Arg	Ser	Gln	Pro	Asp	Pro	Val	Asp	Thr
1490						1495						1500		
Pro	Thr	Ser	Ser	Lys	Pro	Gln	Ser	Lys	Arg	Ser	Leu	Arg	Lys	Val
1505						1510						1515		
Asp	Val	Glu	Glu	Glu	Phe	Phe	Ala	Leu	Arg	Lys	Arg	Thr	Pro	Ser
1520						1525						1530		
Ala	Gly	Lys	Ala	Met	His	Thr	Pro	Lys	Pro	Ala	Val	Ser	Gly	Glu
1535						1540						1545		
Lys	Asn	Ile	Tyr	Ala	Phe	Met	Gly	Thr	Pro	Val	Gln	Lys	Leu	Asp
1550						1555						1560		
Leu	Thr	Glu	Asn	Leu	Thr	Gly	Ser	Lys	Arg	Arg	Leu	Gln	Thr	Pro
1565						1570						1575		

Lys	Glu	Lys	Ala	Gln	Ala	Leu	Glu	Asp	Leu	Ala	Gly	Phe	Lys	Glu
1580						1585					1590			
Leu	Phe	Gln	Thr	Arg	Gly	His	Thr	Glu	Glu	Ser	Met	Thr	Asn	Asp
1595						1600					1605			
Lys	Thr	Ala	Lys	Val	Ala	Cys	Lys	Ser	Ser	Gln	Pro	Asp	Leu	Asp
1610						1615					1620			
Lys	Asn	Pro	Ala	Ser	Ser	Lys	Arg	Arg	Leu	Lys	Thr	Ser	Leu	Gly
1625						1630					1635			
Lys	Val	Gly	Val	Lys	Glu	Glu	Leu	Leu	Ala	Val	Gly	Lys	Leu	Thr
1640						1645					1650			
Gln	Thr	Ser	Gly	Glu	Thr	Thr	His	Thr	His	Thr	Glu	Pro	Thr	Gly
1655						1660					1665			
Asp	Gly	Lys	Ser	Met	Lys	Ala	Phe	Met	Glu	Ser	Pro	Lys	Gln	Ile
1670						1675					1680			
Leu	Asp	Ser	Ala	Ala	Ser	Leu	Thr	Gly	Ser	Lys	Arg	Gln	Leu	Arg
1685						1690					1695			
Thr	Pro	Lys	Gly	Lys	Ser	Glu	Val	Pro	Glu	Asp	Leu	Ala	Gly	Phe
1700						1705					1710			
Ile	Glu	Leu	Phe	Gln	Thr	Pro	Ser	His	Thr	Lys	Glu	Ser	Met	Thr
1715						1720					1725			
Asn	Glu	Lys	Thr	Thr	Lys	Val	Ser	Tyr	Arg	Ala	Ser	Gln	Pro	Asp
1730						1735					1740			
Leu	Val	Asp	Thr	Pro	Thr	Ser	Ser	Lys	Pro	Gln	Pro	Lys	Arg	Ser
1745						1750					1755			
Leu	Arg	Lys	Ala	Asp	Thr	Glu	Glu	Glu	Phe	Leu	Ala	Phe	Arg	Lys
1760						1765					1770			
Gln	Thr	Pro	Ser	Ala	Gly	Lys	Ala	Met	His	Thr	Pro	Lys	Pro	Ala
1775						1780					1785			
Val	Gly	Glu	Glu	Lys	Asp	Ile	Asn	Thr	Phe	Leu	Gly	Thr	Pro	Val
1790						1795					1800			
Gln	Lys	Leu	Asp	Gln	Pro	Gly	Asn	Leu	Pro	Gly	Ser	Asn	Arg	Arg
1805						1810					1815			
Leu	Gln	Thr	Arg	Lys	Glu	Lys	Ala	Gln	Ala	Leu	Glu	Glu	Leu	Thr
1820						1825					1830			
Gly	Phe	Arg	Glu	Leu	Phe	Gln	Thr	Pro	Cys	Thr	Asp	Asn	Pro	Thr
1835						1840					1845			
Ala	Asp	Glu	Lys	Thr	Thr	Lys	Lys	Ile	Leu	Cys	Lys	Ser	Pro	Gln
1850						1855					1860			
Ser	Asp	Pro	Ala	Asp	Thr	Pro	Thr	Asn	Thr	Lys	Gln	Arg	Pro	Lys
1865						1870					1875			
Arg	Ser	Leu	Lys	Lys	Ala	Asp	Val	Glu	Glu	Glu	Phe	Leu	Ala	Phe
1880						1885					1890			
Arg	Lys	Leu	Thr	Pro	Ser	Ala	Gly	Lys	Ala	Met	His	Thr	Pro	Lys
1895						1900					1905			
Ala	Ala	Val	Gly	Glu	Glu	Lys	Asp	Ile	Asn	Thr	Phe	Val	Gly	Thr
1910						1915					1920			
Pro	Val	Glu	Lys	Leu	Asp	Leu	Leu	Gly	Asn	Leu	Pro	Gly	Ser	Lys
1925						1930					1935			
Arg	Arg	Pro	Gln	Thr	Pro	Lys	Glu	Lys	Ala	Lys	Ala	Leu	Glu	Asp
1940						1945					1950			
Leu	Ala	Gly	Phe	Lys	Glu	Leu	Phe	Gln	Thr	Pro	Gly	His	Thr	Glu
1955						1960					1965			
Glu	Ser	Met	Thr	Asp	Asp	Lys	Ile	Thr	Glu	Val	Ser	Cys	Lys	Ser
1970						1975					1980			
Pro	Gln	Pro	Asp	Pro	Val	Lys	Thr	Pro	Thr	Ser	Ser	Lys	Gln	Arg
1985						1990					1995			
Leu	Lys	Ile	Ser	Leu	Gly	Lys	Val	Gly	Val	Lys	Glu	Glu	Val	Leu
2000						2005					2010			
Pro	Val	Gly	Lys	Leu	Thr	Gln	Thr	Ser	Gly	Lys	Thr	Thr	Gln	Thr
2015						2020					2025			
His	Arg	Glu	Thr	Ala	Gly	Asp	Gly	Lys	Ser	Ile	Lys	Ala	Phe	Lys
2030						2035					2040			

Glu	Ser	Ala	Lys	Gln	Met	Leu	Asp	Pro	Ala	Asn	Tyr	Gly	Thr	Gly
2045						2050					2055			
Met	Glu	Arg	Trp	Pro	Arg	Thr	Pro	Lys	Glu	Glu	Ala	Gln	Ser	Leu
2060						2065					2070			
Glu	Asp	Leu	Ala	Gly	Phe	Lys	Glu	Leu	Phe	Gln	Thr	Pro	Asp	His
2075						2080					2085			
Thr	Glu	Glu	Ser	Thr	Thr	Asp	Asp	Lys	Thr	Thr	Lys	Ile	Ala	Cys
2090						2095					2100			
Lys	Ser	Pro	Pro	Pro	Glu	Ser	Met	Asp	Thr	Pro	Thr	Ser	Thr	Arg
2105						2110					2115			
Arg	Arg	Pro	Lys	Thr	Pro	Leu	Gly	Lys	Arg	Asp	Ile	Val	Glu	Glu
2120						2125					2130			
Leu	Ser	Ala	Leu	Lys	Gln	Leu	Thr	Gln	Thr	Thr	His	Thr	Asp	Lys
2135						2140					2145			
Val	Pro	Gly	Asp	Glu	Asp	Lys	Gly	Ile	Asn	Val	Phe	Arg	Glu	Thr
2150						2155					2160			
Ala	Lys	Gln	Lys	Leu	Asp	Pro	Ala	Ala	Ser	Val	Thr	Gly	Ser	Lys
2165						2170					2175			
Arg	Gln	Pro	Arg	Thr	Pro	Lys	Gly	Lys	Ala	Gln	Pro	Leu	Glu	Asp
2180						2185					2190			
Leu	Ala	Gly	Leu	Lys	Glu	Leu	Phe	Gln	Thr	Pro	Val	Cys	Thr	Asp
2195						2200					2205			
Lys	Pro	Thr	Thr	His	Glu	Lys	Thr	Thr	Lys	Ile	Ala	Cys	Arg	Ser
2210						2215					2220			
Pro	Gln	Pro	Asp	Pro	Val	Gly	Thr	Pro	Thr	Ile	Phe	Lys	Pro	Gln
2225						2230					2235			
Ser	Lys	Arg	Ser	Leu	Arg	Lys	Ala	Asp	Val	Glu	Glu	Glu	Ser	Leu
2240						2245					2250			
Ala	Leu	Arg	Lys	Arg	Thr	Pro	Ser	Val	Gly	Lys	Ala	Met	Asp	Thr
2255						2260					2265			
Pro	Lys	Pro	Ala	Gly	Gly	Asp	Glu	Lys	Asp	Met	Lys	Ala	Phe	Met
2270						2275					2280			
Gly	Thr	Pro	Val	Gln	Lys	Leu	Asp	Leu	Pro	Gly	Asn	Leu	Pro	Gly
2285						2290					2295			
Ser	Lys	Arg	Trp	Pro	Gln	Thr	Pro	Lys	Glu	Lys	Ala	Gln	Ala	Leu
2300						2305					2310			
Glu	Asp	Leu	Ala	Gly	Phe	Lys	Glu	Leu	Phe	Gln	Thr	Pro	Gly	Thr
2315						2320					2325			
Asp	Lys	Pro	Thr	Thr	Asp	Glu	Lys	Thr	Thr	Lys	Ile	Ala	Cys	Lys
2330						2335					2340			
Ser	Pro	Gln	Pro	Asp	Pro	Val	Asp	Thr	Pro	Ala	Ser	Thr	Lys	Gln
2345						2350					2355			
Arg	Pro	Lys	Arg	Asn	Leu	Arg	Lys	Ala	Asp	Val	Glu	Glu	Glu	Phe
2360						2365					2370			
Leu	Ala	Leu	Arg	Lys	Arg	Thr	Pro	Ser	Ala	Gly	Lys	Ala	Met	Asp
2375						2380					2385			
Thr	Pro	Lys	Pro	Ala	Val	Ser	Asp	Glu	Lys	Asn	Ile	Asn	Thr	Phe
2390						2395					2400			
Val	Glu	Thr	Pro	Val	Gln	Lys	Leu	Asp	Leu	Leu	Gly	Asn	Leu	Pro
2405						2410					2415			
Gly	Ser	Lys	Arg	Gln	Pro	Gln	Thr	Pro	Lys	Glu	Lys	Ala	Glu	Ala
2420						2425					2430			
Leu	Glu	Asp	Leu	Val	Gly	Phe	Lys	Glu	Leu	Phe	Gln	Thr	Pro	Gly
2435						2440					2445			
His	Thr	Glu	Glu	Ser	Met	Thr	Asp	Asp	Lys	Ile	Thr	Glu	Val	Ser
2450						2455					2460			
Cys	Lys	Ser	Pro	Gln	Pro	Glu	Ser	Phe	Lys	Thr	Ser	Arg	Ser	Ser
2465						2470					2475			
Lys	Gln	Arg	Leu	Lys	Ile	Pro	Leu	Val	Lys	Val	Asp	Met	Lys	Glu
2480						2485					2490			
Glu	Pro	Leu	Ala	Val	Ser	Lys	Leu	Thr	Arg	Thr	Ser	Gly	Glu	Thr
2495						2500					2505			

Thr	Gln	Thr	His	Thr	Glu	Pro	Thr	Gly	Asp	Ser	Lys	Ser	Ile	Lys
2510						2515					2520			
Ala	Phe	Lys	Glu	Ser	Pro	Lys	Gln	Ile	Leu	Asp	Pro	Ala	Ala	Ser
2525						2530					2535			
Val	Thr	Gly	Ser	Arg	Arg	Gln	Leu	Arg	Thr	Arg	Lys	Glu	Lys	Ala
2540						2545					2550			
Arg	Ala	Leu	Glu	Asp	Leu	Val	Asp	Phe	Lys	Glu	Leu	Phe	Ser	Ala
2555						2560					2565			
Pro	Gly	His	Thr	Glu	Glu	Ser	Met	Thr	Ile	Asp	Lys	Asn	Thr	Lys
2570						2575					2580			
Ile	Pro	Cys	Lys	Ser	Pro	Pro	Pro	Glu	Leu	Thr	Asp	Thr	Ala	Thr
2585						2590					2595			
Ser	Thr	Lys	Arg	Cys	Pro	Lys	Thr	Arg	Pro	Arg	Lys	Glu	Val	Lys
2600						2605					2610			
Glu	Glu	Leu	Ser	Ala	Val	Glu	Arg	Leu	Thr	Gln	Thr	Ser	Gly	Gln
2615						2620					2625			
Ser	Thr	His	Thr	His	Lys	Glu	Pro	Ala	Ser	Gly	Asp	Glu	Gly	Ile
2630						2635					2640			
Lys	Val	Leu	Lys	Gln	Arg	Ala	Lys	Lys	Lys	Pro	Asn	Pro	Val	Glu
2645						2650					2655			
Glu	Glu	Pro	Ser	Arg	Arg	Arg	Pro	Arg	Ala	Pro	Lys	Glu	Lys	Ala
2660						2665					2670			
Gln	Pro	Leu	Glu	Asp	Leu	Ala	Gly	Phe	Thr	Glu	Leu	Ser	Glu	Thr
2675						2680					2685			
Ser	Gly	His	Thr	Gln	Glu	Ser	Leu	Thr	Ala	Gly	Lys	Ala	Thr	Lys
2690						2695					2700			
Ile	Pro	Cys	Glu	Ser	Pro	Pro	Leu	Glu	Val	Val	Asp	Thr	Thr	Ala
2705						2710					2715			
Ser	Thr	Lys	Arg	His	Leu	Arg	Thr	Arg	Val	Gln	Lys	Val	Gln	Val
2720						2725					2730			
Lys	Glu	Glu	Pro	Ser	Ala	Val	Lys	Phe	Thr	Gln	Thr	Ser	Gly	Glu
2735						2740					2745			
Thr	Thr	Asp	Ala	Asp	Lys	Glu	Pro	Ala	Gly	Glu	Asp	Lys	Gly	Ile
2750						2755					2760			
Lys	Ala	Leu	Lys	Glu	Ser	Ala	Lys	Gln	Thr	Pro	Ala	Pro	Ala	Ala
2765						2770					2775			
Ser	Val	Thr	Gly	Ser	Arg	Arg	Arg	Pro	Arg	Ala	Pro	Arg	Glu	Ser
2780						2785					2790			
Ala	Gln	Ala	Ile	Glu	Asp	Leu	Ala	Gly	Phe	Lys	Asp	Pro	Ala	Ala
2795						2800					2805			
Gly	His	Thr	Glu	Glu	Ser	Met	Thr	Asp	Asp	Lys	Thr	Thr	Lys	Ile
2810						2815					2820			
Pro	Cys	Lys	Ser	Ser	Pro	Glu	Leu	Glu	Asp	Thr	Ala	Thr	Ser	Ser
2825						2830					2835			
Lys	Arg	Arg	Pro	Arg	Thr	Arg	Ala	Gln	Lys	Val	Glu	Val	Lys	Glu
2840						2845					2850			
Glu	Leu	Leu	Ala	Val	Gly	Lys	Leu	Thr	Gln	Thr	Ser	Gly	Glu	Thr
2855						2860					2865			
Thr	His	Thr	Asp	Lys	Glu	Pro	Val	Gly	Glu	Gly	Lys	Gly	Thr	Lys
2870						2875					2880			
Ala	Phe	Lys	Gln	Pro	Ala	Lys	Arg	Asn	Val	Asp	Ala	Glu	Asp	Val
2885						2890					2895			
Ile	Gly	Ser	Arg	Arg	Gln	Pro	Arg	Ala	Pro	Lys	Glu	Lys	Ala	Gln
2900						2905					2910			
Pro	Leu	Glu	Asp	Leu	Ala	Ser	Phe	Gln	Glu	Leu	Ser	Gln	Thr	Pro
2915						2920					2925			
Gly	His	Thr	Glu	Glu	Leu	Ala	Asn	Gly	Ala	Ala	Asp	Ser	Phe	Thr
2930						2935					2940			
Ser	Ala	Pro	Lys	Gln	Thr	Pro	Asp	Ser	Gly	Lys	Pro	Leu	Lys	Ile
2945						2950					2955			
Ser	Arg	Arg	Val	Leu	Arg	Ala	Pro	Lys	Val	Glu	Pro	Val	Gly	Asp
2960						2965					2970			

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Val	Val	Ser	Thr	Arg	Asp	Pro	Val	Lys	Ser	Gln	Ser	Lys	Ser	Asn
2975						2980					2985			
Thr	Ser	Leu	Pro	Pro	Leu	Pro	Phe	Lys	Arg	Gly	Gly	Gly	Lys	Asp
2990						2995					3000			
Gly	Ser	Val	Thr	Gly	Thr	Lys	Arg	Leu	Arg	Cys	Met	Pro	Ala	Pro
3005						3010					3015			
Glu	Glu	Ile	Val	Glu	Glu	Leu	Pro	Ala	Ser	Lys	Lys	Gln	Arg	Val
3020						3025					3030			
Ala	Pro	Arg	Ala	Arg	Gly	Lys	Ser	Ser	Glu	Pro	Val	Val	Ile	Met
3035						3040					3045			
Lys	Arg	Ser	Leu	Arg	Thr	Ser	Ala	Lys	Arg	Ile	Glu	Pro	Ala	Glu
3050						3055					3060			
Glu	Leu	Asn	Ser	Asn	Asp	Met	Lys	Thr	Asn	Lys	Glu	Glu	His	Lys
3065						3070					3075			
Leu	Gln	Asp	Ser	Val	Pro	Glu	Asn	Lys	Gly	Ile	Ser	Leu	Arg	Ser
3080						3085					3090			
Arg	Arg	Gln	Asp	Lys	Thr	Glu	Ala	Glu	Gln	Gln	Ile	Thr	Glu	Val
3095						3100					3105			
Phe	Val	Leu	Ala	Glu	Arg	Ile	Glu	Ile	Asn	Arg	Asn	Glu	Lys	Lys
3110						3115					3120			
Pro	Met	Lys	Thr	Ser	Pro	Glu	Met	Asp	Ile	Gln	Asn	Pro	Asp	Asp
3125						3130					3135			
Gly	Ala	Arg	Lys	Pro	Ile	Pro	Arg	Asp	Lys	Val	Thr	Glu	Asn	Lys
3140						3145					3150			
Arg	Cys	Leu	Arg	Ser	Ala	Arg	Gln	Asn	Glu	Ser	Ser	Gln	Pro	Lys
3155						3160					3165			
Val	Ala	Glu	Glu	Ser	Gly	Gly	Gln	Lys	Ser	Ala	Lys	Val	Leu	Met
3170						3175					3180			
Gln	Asn	Gln	Lys	Gly	Lys	Gly	Glu	Ala	Gly	Asn	Ser	Asp	Ser	Met
3185						3190					3195			
Cys	Leu	Arg	Ser	Arg	Lys	Thr	Lys	Ser	Gln	Pro	Ala	Ala	Ser	Thr
3200						3205					3210			
Leu	Glu	Ser	Lys	Ser	Val	Gln	Arg	Val	Thr	Arg	Ser	Val	Lys	Arg
3215						3220					3225			
Cys	Ala	Glu	Asn	Pro	Lys	Lys	Ala	Glu	Asp	Asn	Val	Cys	Val	Lys
3230						3235					3240			
Lys	Ile	Thr	Thr	Arg	Ser	His	Arg	Asp	Ser	Glu	Asp	Ile		
3245						3250					3255			

&lt;210&gt; 258

&lt;211&gt; 160

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 258

Met	Ser	Glu	Val	Arg	Pro	Leu	Ser	Arg	Asp	Ile	Leu	Met	Glu	Thr	Leu
1			5					10					15		
Leu	Tyr	Glu	Gln	Leu	Leu	Glu	Pro	Pro	Thr	Met	Glu	Val	Leu	Gly	Met
		20					25					30			
Thr	Asp	Ser	Glu	Glu	Asp	Leu	Asp	Pro	Met	Glu	Asp	Phe	Asp	Ser	Leu
	35					40					45				
Glu	Cys	Met	Glu	Gly	Ser	Asp	Ala	Leu	Ala	Leu	Arg	Leu	Ala	Cys	Ile
	50				55				60						
Gly	Asp	Glu	Met	Asp	Val	Ser	Leu	Arg	Ala	Pro	Arg	Leu	Ala	Gln	Leu
65				70				75					80		
Ser	Glu	Val	Ala	Met	His	Ser	Leu	Gly	Leu	Ala	Phe	Ile	Tyr	Asp	Gln
			85					90					95		

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Thr Glu Asp Ile Arg Asp Val Leu Arg Ser Phe Met Asp Gly Phe Thr  
 100 105 110  
 Thr Leu Lys Glu Asn Ile Met Arg Phe Trp Arg Ser Pro Asn Pro Gly  
 115 120 125  
 Ser Trp Val Ser Cys Glu Gln Val Leu Leu Ala Leu Leu Leu Leu  
 130 135 140  
 Ala Leu Leu Leu Pro Leu Leu Ser Gly Gly Leu His Leu Leu Leu Lys  
 145 150 155 160

&lt;210&gt; 259

&lt;211&gt; 1844

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 259

Met Thr Thr Arg Phe Thr Asp Glu Leu Met Glu Gln Gly Leu Thr Tyr  
 1 5 10 15  
 Lys Val Leu Thr Leu Val Ser Gln Ile Asp Val Asn Asn Glu Phe Glu  
 20 25 30  
 Lys Leu Gln Arg Glu Arg Gly Leu Gly Ser Glu Lys His Arg Lys Glu  
 35 40 45  
 Val Ser Asp Leu Ile Lys Glu Cys Arg Gln Ser Leu Ala Glu Ser Leu  
 50 55 60  
 Phe Ala Trp Ala Cys Gln Ser Pro Leu Gly Lys Glu Asp Thr Leu Leu  
 65 70 75 80  
 Leu Ile Gly His Leu Glu Arg Val Thr Val Glu Ala Asn Gly Ser Leu  
 85 90 95  
 Asp Ala Val Asn Leu Ala Leu Leu Met Ala Leu Leu Tyr Cys Phe Asp  
 100 105 110  
 Ile Ser Phe Ile Glu Gln Ser Thr Glu Glu Arg Asp Asp Met Ile His  
 115 120 125  
 Gln Leu Pro Leu Leu Thr Glu Lys Gln Tyr Ile Ala Thr Ile His Ser  
 130 135 140  
 Arg Leu Gln Asp Ser Gln Leu Trp Lys Leu Pro Gly Leu Gln Ala Thr  
 145 150 155 160  
 Val Arg Leu Ala Trp Ala Leu Ala Leu Arg Gly Ile Ser Gln Leu Pro  
 165 170 175  
 Asp Val Thr Ala Leu Ala Glu Phe Thr Glu Ala Asp Glu Ala Met Ala  
 180 185 190  
 Glu Leu Ala Ile Ala Asp Asn Val Phe Leu Phe Leu Met Glu Ser Val  
 195 200 205  
 Val Val Ser Glu Tyr Phe Tyr Gln Glu Glu Phe Tyr Ile Arg Arg Val  
 210 215 220  
 His Asn Leu Ile Thr Asp Phe Leu Ala Leu Met Pro Met Lys Val Lys  
 225 230 235 240  
 Gln Leu Arg Asn Arg Ala Asp Glu Asp Ala Arg Met Ile His Met Ser  
 245 250 255  
 Met Gln Met Gly Asn Glu Pro Pro Ile Ser Leu Arg Arg Asp Leu Glu  
 260 265 270  
 His Leu Met Leu Leu Ile Gly Glu Leu Tyr Lys Lys Asn Pro Phe His  
 275 280 285  
 Leu Glu Leu Ala Leu Glu Tyr Trp Cys Pro Thr Glu Pro Leu Gln Thr  
 290 295 300  
 Pro Thr Ile Met Gly Ser Tyr Leu Gly Val Ala His Gln Arg Pro Pro  
 305 310 315 320  
 Gln Arg Gln Val Val Leu Ser Lys Phe Val Arg Gln Met Gly Asp Leu  
 325 330 335

Leu	Pro	Pro	Thr	Ile	Tyr	Ile	Pro	Tyr	Leu	Lys	Met	Leu	Gln	Gly	Leu
			340					345					350		
Ala	Asn	Gly	Pro	Gln	Cys	Ala	His	Tyr	Cys	Phe	Ser	Leu	Leu	Lys	Val
		355					360					365			
Asn	Gly	Ser	Ser	His	Val	Glu	Asn	Ile	Gln	Gly	Ala	Gly	Gly	Ser	Pro
	370					375				380					
Val	Ser	Trp	Glu	His	Phe	Phe	His	Ser	Leu	Met	Leu	Tyr	His	Glu	His
385					390					395					400
Leu	Arg	Lys	Asp	Leu	Pro	Ser	Ala	Asp	Ser	Val	Gln	Tyr	Arg	His	Leu
			405					410						415	
Pro	Ser	Arg	Gly	Ile	Thr	Gln	Lys	Glu	Gln	Asp	Gly	Leu	Ile	Ala	Phe
			420					425					430		
Leu	Gln	Leu	Thr	Ser	Thr	Ile	Ile	Thr	Trp	Ser	Glu	Asn	Ala	Arg	Leu
	435						440					445			
Ala	Leu	Cys	Glu	His	Pro	Gln	Trp	Thr	Pro	Val	Val	Val	Ile	Leu	Gly
	450					455				460					
Leu	Leu	Gln	Cys	Ser	Ile	Pro	Pro	Val	Leu	Lys	Ala	Glu	Leu	Leu	Lys
465					470					475					480
Thr	Leu	Ala	Ala	Phe	Gly	Lys	Ser	Pro	Glu	Ile	Ala	Ala	Ser	Leu	Trp
				485					490						495
Gln	Ser	Leu	Glu	Tyr	Thr	Gln	Ile	Leu	Gln	Thr	Val	Arg	Ile	Pro	Ser
			500					505					510		
Gln	Arg	Gln	Ala	Ile	Gly	Ile	Glu	Val	Glu	Leu	Asn	Glu	Ile	Glu	Ser
	515						520					525			
Arg	Cys	Glu	Glu	Tyr	Pro	Leu	Thr	Arg	Ala	Phe	Cys	Gln	Leu	Ile	Ser
	530					535					540				
Thr	Leu	Val	Glu	Ser	Ser	Phe	Pro	Ser	Asn	Leu	Gly	Ala	Gly	Leu	Arg
545					550					555					560
Pro	Pro	Gly	Phe	Asp	Pro	Tyr	Leu	Gln	Phe	Leu	Arg	Asp	Ser	Val	Phe
			565						570						575
Leu	Arg	Phe	Arg	Thr	Arg	Ala	Tyr	Arg	Arg	Ala	Ala	Glu	Lys	Trp	Glu
			580					585					590		
Val	Ala	Glu	Val	Val	Leu	Glu	Val	Phe	Tyr	Lys	Leu	Leu	Arg	Asp	Tyr
		595					600					605			
Glu	Pro	Gln	Leu	Glu	Asp	Phe	Val	Asp	Gln	Phe	Val	Glu	Leu	Gln	Gly
	610					615					620				
Glu	Glu	Ile	Ile	Ala	Tyr	Lys	Pro	Pro	Gly	Phe	Ser	Leu	Met	Tyr	His
625					630					635					640
Leu	Leu	Asn	Glu	Ser	Pro	Met	Leu	Glu	Leu	Ala	Leu	Ser	Leu	Leu	Glu
				645					650						655
Glu	Gly	Val	Lys	Gln	Leu	Asp	Thr	Tyr	Ala	Pro	Phe	Pro	Gly	Lys	Lys
			660					665					670		
His	Leu	Glu	Lys	Ala	Val	Gln	His	Cys	Leu	Ala	Leu	Leu	Asn	Leu	Thr
		675					680					685			
Leu	Gln	Lys	Glu	Asn	Leu	Phe	Met	Asp	Leu	Leu	Arg	Glu	Ser	Gln	Leu
	690					695					700				
Ala	Leu	Ile	Val	Cys	Pro	Leu	Glu	Gln	Leu	Leu	Gln	Gly	Ile	Asn	Pro
705					710					715					720
Arg	Thr	Lys	Lys	Ala	Asp	Asn	Val	Val	Asn	Ile	Ala	Arg	Tyr	Leu	Tyr
				725					730						735
His	Gly	Asn	Thr	Asn	Pro	Glu	Leu	Ala	Phe	Glu	Ser	Ala	Lys	Ile	Leu
			740					745					750		
Cys	Cys	Ile	Ser	Cys	Asn	Ser	Asn	Ile	Gln	Ile	Lys	Leu	Val	Gly	Asp
		755					760					765			
Phe	Thr	His	Asp	Gln	Ser	Ile	Ser	Gln	Lys	Leu	Met	Ala	Gly	Phe	Val
	770					775					780				
Glu	Cys	Leu	Asp	Cys	Glu	Asp	Ala	Glu	Glu	Phe	Val	Arg	Leu	Glu	Glu
785					790					795					800
Gly	Ser	Glu	Leu	Glu	Lys	Lys	Leu	Val	Ala	Ile	Arg	His	Glu	Thr	Arg
				805					810					815	
Ile	His	Ile	Leu	Asn	Leu	Leu	Ile	Thr	Ser	Leu	Glu	Cys	Asn	Pro	Pro
			820					825					830		



Asn Leu Ala Leu Tyr Leu Leu Gly Phe Glu Leu Lys Lys Pro Val Ser  
 835 840 845  
 Thr Thr Asn Leu Gln Asp Pro Gly Val Leu Gly Cys Pro Arg Thr Cys  
 850 855 860  
 Leu His Ala Ile Leu Asn Ile Leu Glu Lys Gly Thr Glu Gly Arg Thr  
 865 870 875 880  
 Gly Pro Val Ala Val Arg Glu Ser Pro Gln Leu Ala Glu Leu Cys Tyr  
 885 890 895  
 Gln Val Ile Tyr Gln Leu Cys Ala Cys Ser Asp Thr Ser Gly Pro Thr  
 900 905 910  
 Met Arg Tyr Leu Arg Thr Ser Gln Asp Phe Leu Phe Ser Gln Leu Gln  
 915 920 925  
 Tyr Leu Pro Phe Ser Asn Lys Glu Tyr Glu Ile Ser Met Leu Asn Gln  
 930 935 940  
 Met Ser Trp Leu Met Lys Thr Ala Ser Ile Glu Leu Arg Val Thr Ser  
 945 950 955 960  
 Leu Asn Arg Gln Arg Ser His Thr Gln Arg Leu Leu His Leu Leu  
 965 970 975  
 Asp Asp Met Pro Val Lys Pro Tyr Ser Asp Gly Glu Gly Gly Ile Glu  
 980 985 990  
 Asp Glu Asn Arg Ser Val Ser Gly Phe Leu His Phe Asp Thr Ala Thr  
 995 1000 1005  
 Lys Val Arg Arg Lys Ile Leu Asn Ile Leu Asp Ser Ile Asp Phe  
 1010 1015 1020  
 Ser Gln Glu Ile Pro Glu Pro Leu Gln Leu Asp Phe Phe Asp Arg  
 1025 1030 1035  
 Ala Gln Ile Glu Gln Val Ile Ala Asn Cys Glu His Lys Asn Leu  
 1040 1045 1050  
 Arg Gly Gln Thr Val Cys Asn Val Lys Leu Leu His Arg Val Leu  
 1055 1060 1065  
 Val Ala Glu Val Asn Ala Leu Gln Gly Met Ala Ala Ile Gly Gln  
 1070 1075 1080  
 Arg Pro Leu Leu Met Glu Glu Ile Ser Thr Val Leu Gln Tyr Val  
 1085 1090 1095  
 Val Gly Arg Asn Lys Leu Leu Gln Cys Leu His Ala Lys Arg His  
 1100 1105 1110  
 Ala Leu Glu Ser Trp Arg Gln Leu Val Glu Ile Ile Leu Thr Ala  
 1115 1120 1125  
 Cys Pro Gln Asp Leu Ile Gln Ala Glu Asp Arg Gln Leu Ile Ile  
 1130 1135 1140  
 Arg Asp Ile Leu Gln Asp Val His Asp Lys Ile Leu Asp Asp Glu  
 1145 1150 1155  
 Ala Ala Gln Glu Leu Met Pro Val Val Ala Gly Ala Val Phe Thr  
 1160 1165 1170  
 Leu Thr Ala His Leu Ser Gln Ala Val Leu Thr Glu Gln Lys Glu  
 1175 1180 1185  
 Thr Ser Val Leu Gly Pro Ala Glu Ala His Tyr Ala Phe Met Leu  
 1190 1195 1200  
 Asp Ser Cys Phe Thr Ser Pro Pro Pro Glu Glu Asn Pro Leu Val  
 1205 1210 1215  
 Gly Phe Ala Ser Ile Gly Asp Ser Ser Leu Tyr Ile Ile Leu Lys  
 1220 1225 1230  
 Lys Leu Leu Asp Phe Ile Leu Lys Thr Gly Gly Gly Phe Gln Arg  
 1235 1240 1245  
 Val Arg Thr His Leu Tyr Gly Ser Leu Leu Tyr Tyr Leu Gln Ile  
 1250 1255 1260  
 Ala Gln Arg Pro Asp Glu Pro Asp Thr Leu Glu Ala Lys Lys  
 1265 1270 1275  
 Thr Met Trp Glu Arg Leu Thr Ala Pro Glu Asp Val Phe Ser Lys  
 1280 1285 1290  
 Leu Gln Arg Glu Asn Ile Ala Ile Ile Glu Ser Tyr Gly Ala Ala  
 1295 1300 1305

Leu	Met	Glu	Val	Val	Cys	Arg	Asp	Ala	Cys	Asp	Gly	His	Glu	Ile
1310						1315					1320			
Gly	Arg	Met	Leu	Ala	Leu	Ala	Leu	Leu	Asp	Arg	Ile	Val	Ser	Val
1325						1330					1335			
Asp	Lys	Gln	Gln	Gln	Trp	Leu	Leu	Tyr	Leu	Ser	Asn	Ser	Gly	Tyr
1340						1345					1350			
Leu	Lys	Val	Leu	Val	Asp	Ser	Leu	Val	Glu	Asp	Asp	Arg	Thr	Leu
1355						1360					1365			
Gln	Ser	Leu	Leu	Thr	Pro	Gln	Pro	Pro	Leu	Leu	Lys	Ala	Leu	Tyr
1370						1375					1380			
Thr	Tyr	Glu	Ser	Lys	Met	Ala	Phe	Leu	Thr	Arg	Val	Ala	Lys	Ile
1385						1390					1395			
Gln	Gln	Gly	Ala	Leu	Glu	Leu	Leu	Arg	Ser	Gly	Val	Ile	Val	Arg
1400						1405					1410			
Leu	Ala	Gln	Cys	Gln	Val	Tyr	Asp	Met	Arg	Pro	Glu	Thr	Asp	Pro
1415						1420					1425			
Gln	Ser	Met	Phe	Gly	Met	Arg	Asp	Pro	Pro	Met	Phe	Ile	Pro	Thr
1430						1435					1440			
Pro	Val	Asp	Arg	Tyr	Arg	Gln	Ile	Leu	Leu	Pro	Ala	Leu	Gln	Leu
1445						1450					1455			
Cys	Gln	Val	Ile	Leu	Thr	Ser	Ser	Met	Ala	Gln	His	Leu	Gln	Ala
1460						1465					1470			
Ala	Gly	Gln	Val	Leu	Gln	Phe	Leu	Ile	Ser	His	Ser	Asp	Thr	Ile
1475						1480					1485			
Gln	Ala	Ile	Leu	Arg	Cys	Gln	Asp	Val	Ser	Ala	Gly	Ser	Leu	Gln
1490						1495					1500			
Glu	Leu	Ala	Leu	Leu	Thr	Gly	Ile	Ile	Ser	Lys	Ala	Ala	Leu	Pro
1505						1510					1515			
Gly	Ile	Leu	Ser	Glu	Leu	Asp	Val	Asp	Val	Asn	Glu	Gly	Ser	Leu
1520						1525					1530			
Met	Glu	Leu	Gln	Gly	His	Ile	Gly	Arg	Phe	Gln	Arg	Gln	Cys	Leu
1535						1540					1545			
Gly	Leu	Leu	Ser	Arg	Phe	Gly	Gly	Ser	Asp	Arg	Leu	Arg	Gln	Phe
1550						1555					1560			
Lys	Phe	Gln	Asp	Asp	Asn	Val	Glu	Gly	Asp	Lys	Val	Ser	Lys	Lys
1565						1570					1575			
Asp	Glu	Ile	Glu	Leu	Ala	Met	Gln	Gln	Ile	Cys	Ala	Asn	Val	Met
1580						1585					1590			
Glu	Tyr	Cys	Gln	Ser	Leu	Met	Leu	Gln	Ser	Ser	Pro	Thr	Phe	Gln
1595						1600					1605			
His	Ala	Val	Cys	Leu	Phe	Thr	Pro	Ser	Leu	Ser	Glu	Thr	Val	Asn
1610						1615					1620			
Arg	Asp	Gly	Pro	Arg	Gln	Asp	Thr	Gln	Ala	Pro	Val	Val	Pro	Tyr
1625						1630					1635			
Trp	Arg	Leu	Pro	Gly	Leu	Gly	Ile	Ile	Ile	Tyr	Leu	Leu	Lys	Gln
1640						1645					1650			
Ser	Ala	Asn	Asp	Phe	Phe	Ser	Tyr	Tyr	Asp	Ser	His	Arg	Gln	Ser
1655						1660					1665			
Val	Ser	Lys	Leu	Gln	Asn	Val	Glu	Gln	Leu	Pro	Pro	Asp	Glu	Ile
1670						1675					1680			
Lys	Glu	Leu	Cys	Gln	Ser	Val	Met	Pro	Ala	Gly	Val	Asp	Lys	Ile
1685						1690					1695			
Ser	Thr	Ala	Gln	Lys	Tyr	Val	Leu	Ala	Arg	Arg	Arg	Leu	Val	Lys
1700						1705					1710			
Val	Ile	Asn	Asn	Arg	Ala	Lys	Leu	Leu	Ser	Leu	Cys	Ser	Phe	Ile
1715						1720					1725			
Ile	Glu	Thr	Cys	Leu	Phe	Ile	Leu	Trp	Arg	His	Leu	Glu	Tyr	Tyr
1730						1735					1740			
Leu	Leu	His	Cys	Met	Pro	Thr	Asp	Ser	Gln	Asp	Ser	Leu	Phe	Ala
1745						1750					1755			
Ser	Arg	Thr	Leu	Phe	Lys	Ser	Arg	Arg	Leu	Gln	Asp	Ser	Phe	Ala
1760						1765					1770			

Ser Glu Thr Asn Leu Asp Phe Arg Ser Gly Leu Ala Ile Val Ser  
 1775 1780 1785  
 Gln His Asp Leu Asp Gln Leu Gln Ala Asp Ala Ile Asn Ala Phe  
 1790 1795 1800  
 Gly Glu Ser Leu Gln Lys Lys Leu Leu Asp Ile Glu Gly Leu Tyr  
 1805 1810 1815  
 Ser Lys Val Arg Ser Arg Tyr Ser Phe Ile Gln Ala Leu Val Arg  
 1820 1825 1830  
 Arg Ile Arg Gly Leu Leu Arg Ile Ser Arg Asn  
 1835 1840

&lt;210&gt; 260

&lt;211&gt; 1299

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 260  
 Met Ala Ala Glu Thr Gln Thr Leu Asn Phe Gly Pro Glu Trp Leu Arg  
 1 5 10 15  
 Ala Leu Ser Ser Gly Gly Ser Ile Thr Ser Pro Pro Leu Ser Pro Ala  
 20 25 30  
 Leu Pro Lys Tyr Lys Leu Ala Asp Tyr Arg Tyr Gly Arg Glu Glu Met  
 35 40 45  
 Leu Ala Leu Phe Leu Lys Asp Asn Lys Ile Pro Ser Asp Leu Leu Asp  
 50 55 60  
 Lys Glu Phe Leu Pro Ile Leu Gln Glu Glu Pro Leu Pro Pro Leu Ala  
 65 70 75 80  
 Leu Val Pro Phe Thr Glu Glu Glu Gln Arg Asn Phe Ser Met Ser Val  
 85 90 95  
 Asn Ser Ala Ala Val Leu Arg Leu Thr Gly Arg Gly Gly Gly Thr  
 100 105 110  
 Val Val Gly Ala Pro Arg Gly Arg Ser Ser Ser Arg Gly Arg Gly Arg  
 115 120 125  
 Gly Arg Gly Glu Cys Gly Phe Tyr Gln Arg Ser Phe Asp Glu Val Glu  
 130 135 140  
 Gly Val Phe Gly Arg Gly Gly Gly Arg Glu Met His Arg Ser Gln Ser  
 145 150 155 160  
 Trp Glu Glu Arg Gly Asp Arg Arg Phe Glu Lys Pro Gly Arg Lys Asp  
 165 170 175  
 Val Gly Arg Pro Asn Phe Glu Glu Gly Gly Pro Thr Ser Val Gly Arg  
 180 185 190  
 Lys His Glu Phe Ile Arg Ser Glu Ser Glu Asn Trp Arg Ile Phe Arg  
 195 200 205  
 Glu Glu Gln Asn Gly Glu Asp Glu Asp Gly Gly Trp Arg Leu Ala Gly  
 210 215 220  
 Ser Arg Arg Asp Gly Glu Arg Trp Arg Pro His Ser Pro Asp Gly Pro  
 225 230 235 240  
 Arg Ser Ala Gly Trp Arg Glu His Met Glu Arg Arg Arg Arg Phe Glu  
 245 250 255  
 Phe Asp Phe Arg Asp Arg Asp Asp Glu Arg Gly Tyr Arg Arg Val Arg  
 260 265 270  
 Ser Gly Ser Gly Ser Ile Asp Asp Arg Asp Ser Leu Pro Glu Trp  
 275 280 285  
 Cys Leu Glu Asp Ala Glu Glu Glu Met Gly Thr Phe Asp Ser Ser Gly  
 290 295 300  
 Ala Phe Leu Ser Leu Lys Lys Val Gln Lys Glu Pro Ile Pro Glu Glu  
 305 310 315 320

Gln Glu Met Asp Phe Arg Pro Val Asp Glu Gly Glu Glu Cys Ser Asp  
 325 330 335  
 Ser Glu Gly Ser His Asn Glu Glu Ala Lys Glu Pro Asp Lys Thr Asn  
 340 345 350  
 Lys Lys Glu Gly Glu Lys Thr Asp Arg Val Gly Val Glu Ala Ser Glu  
 355 360 365  
 Glu Thr Pro Gln Thr Ser Ser Ser Ser Ala Arg Pro Gly Thr Pro Ser  
 370 375 380  
 Asp His Gln Ser Gln Glu Ala Ser Gln Phe Glu Arg Lys Asp Glu Pro  
 385 390 400  
 Lys Thr Glu Gln Thr Glu Lys Ala Glu Glu Thr Arg Met Glu Asn  
 405 410 415  
 Ser Leu Pro Ala Lys Val Pro Ser Arg Gly Asp Glu Met Val Ala Asp  
 420 425 430  
 Val Gln Gln Pro Leu Ser Gln Ile Pro Ser Asp Thr Ala Ser Pro Leu  
 435 440 445  
 Leu Ile Leu Pro Pro Pro Val Asn Pro Ser Pro Thr Leu Arg Pro  
 450 455 460  
 Val Glu Thr Pro Val Val Gly Ala Pro Gly Met Gly Ser Val Ser Thr  
 465 470 475 480  
 Glu Pro Asp Asp Glu Glu Gly Leu Lys His Leu Glu Gln Gln Ala Glu  
 485 490 495  
 Lys Met Val Ala Tyr Leu Gln Asp Ser Ala Leu Asp Asp Glu Arg Leu  
 500 505 510  
 Ala Ser Lys Leu Gln Glu His Arg Ala Lys Gly Val Ser Ile Pro Leu  
 515 520 525  
 Met His Glu Ala Met Gln Lys Trp Tyr Tyr Lys Asp Pro Gln Gly Glu  
 530 535 540  
 Ile Gln Gly Pro Phe Asn Asn Gln Glu Met Ala Glu Trp Phe Gln Ala  
 545 550 555 560  
 Gly Tyr Phe Thr Met Ser Leu Leu Val Lys Arg Ala Cys Asp Glu Ser  
 565 570 575  
 Phe Gln Pro Leu Gly Asp Ile Met Lys Met Trp Gly Arg Val Pro Phe  
 580 585 590  
 Ser Pro Gly Pro Ala Pro Pro Pro His Met Gly Glu Leu Asp Gln Glu  
 595 600 605  
 Arg Leu Thr Arg Gln Gln Glu Leu Thr Ala Leu Tyr Gln Met Gln His  
 610 615 620  
 Leu Gln Tyr Gln Gln Phe Leu Ile Gln Gln Gln Tyr Ala Gln Val Leu  
 625 630 635 640  
 Ala Gln Gln Gln Lys Ala Ala Leu Ser Ser Gln Gln Gln Gln Gln Leu  
 645 650 655  
 Ala Leu Leu Leu Gln Gln Phe Gln Thr Leu Lys Met Arg Ile Ser Asp  
 660 665 670  
 Gln Asn Ile Ile Pro Ser Val Thr Arg Ser Val Ser Val Pro Asp Thr  
 675 680 685  
 Gly Ser Ile Trp Glu Leu Gln Pro Thr Ala Ser Gln Pro Thr Val Trp  
 690 695 700  
 Glu Gly Gly Ser Val Trp Asp Leu Pro Leu Asp Thr Thr Thr Pro Gly  
 705 710 715 720  
 Pro Ala Leu Glu Gln Leu Gln Gln Leu Glu Lys Ala Lys Ala Ala Lys  
 725 730 735  
 Leu Glu Gln Glu Arg Arg Glu Ala Glu Met Arg Ala Lys Arg Glu Glu  
 740 745 750  
 Glu Glu Arg Lys Arg Gln Glu Glu Leu Arg Arg Gln Gln Glu Glu Ile  
 755 760 765  
 Leu Arg Arg Gln Gln Glu Glu Arg Lys Arg Arg Glu Glu Glu Glu  
 770 775 780  
 Leu Ala Arg Arg Lys Gln Glu Gly Ala Leu Arg Arg Gln Arg Glu Gln  
 785 790 795 800  
 Glu Ile Ala Leu Arg Arg Gln Arg Glu Glu Glu Arg Gln Gln Gln  
 805 810 815



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Phe Ser Val Asn Ala Ser Ser Glu Arg Leu Asn Met Gly Glu Ile  
 1280 1285 1290  
 Glu Thr Leu Asp Asp Tyr  
 1295

&lt;210&gt; 261

&lt;211&gt; 107

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 261

Met Ser Gly Cys Arg Val Phe Ile Gly Arg Leu Asn Pro Ala Ala Arg  
 1 5 10 15  
 Glu Lys Asp Val Glu Arg Phe Phe Lys Gly Tyr Gly Arg Ile Arg Asp  
 20 25 30  
 Ile Asp Leu Lys Arg Gly Phe Gly Phe Val Glu Phe Glu Asp Pro Arg  
 35 40 45  
 Asp Ala Asp Asp Ala Val Tyr Glu Leu Asp Gly Lys Glu Leu Cys Ser  
 50 55 60  
 Glu Arg Val Thr Ile Glu His Ala Arg Ala Arg Ser Arg Gly Gly Arg  
 65 70 75 80  
 Gly Arg Gly Arg Tyr Ser Asp Arg Phe Ser Ser Arg Arg Pro Arg Asn  
 85 90 95  
 Asp Arg Arg Tyr Val Lys Gly Gly Trp Leu His  
 100 105

&lt;210&gt; 262

&lt;211&gt; 184

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 262

Met Val Arg Tyr Ser Leu Asp Pro Glu Asn Pro Thr Lys Ser Cys Lys  
 1 5 10 15  
 Ser Arg Gly Ser Asn Leu Arg Val His Phe Lys Asn Thr Arg Glu Thr  
 20 25 30  
 Ala Gln Ala Ile Lys Gly Met His Ile Arg Lys Ala Thr Lys Tyr Leu  
 35 40 45  
 Lys Asp Val Thr Leu Gln Lys Gln Cys Val Pro Phe Arg Arg Tyr Asn  
 50 55 60  
 Gly Gly Val Gly Arg Cys Ala Gln Ala Lys Gln Trp Gly Trp Thr Gln  
 65 70 75 80  
 Gly Arg Trp Pro Lys Lys Ser Ala Glu Phe Leu Leu His Met Leu Lys  
 85 90 95  
 Asn Ala Glu Ser Asn Ala Glu Leu Lys Gly Leu Asp Val Asp Ser Leu  
 100 105 110  
 Val Ile Glu His Ile Gln Val Asn Lys Ala Pro Lys Met Arg Arg Arg  
 115 120 125  
 Thr Tyr Arg Ala His Gly Arg Ile Asn Pro Tyr Met Ser Ser Pro Cys  
 130 135 140  
 His Ile Glu Met Ile Leu Thr Glu Lys Glu Gln Ile Val Pro Lys Pro  
 145 150 155 160

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Glu Glu Glu Val Ala Gln Lys Lys Lys Ile Ser Gln Lys Lys Leu Lys  
 165 170 175  
 Lys Gln Lys Leu Met Ala Arg Glu  
 180

&lt;210&gt; 263

&lt;211&gt; 72

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 263

Met Ser Ser Lys Thr Ala Ser Thr Asn Asn Ile Ala Gln Ala Arg Arg  
 1 5 10 15  
 Thr Val Gln Gln Leu Arg Leu Glu Ala Ser Ile Glu Arg Ile Lys Val  
 20 25 30  
 Ser Lys Ala Ser Ala Asp Leu Met Ser Tyr Cys Glu Glu His Ala Arg  
 35 40 45  
 Ser Asp Pro Leu Leu Ile Gly Ile Pro Thr Ser Glu Asn Pro Phe Lys  
 50 55 60  
 Asp Lys Lys Thr Cys Ile Ile Leu  
 65 70

&lt;210&gt; 264

&lt;211&gt; 462

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 264

Met Lys Thr Arg Arg Thr Thr Arg Leu Gln Gln Gln His Ser Glu Gln  
 1 5 10 15  
 Pro Pro Leu Gln Pro Ser Pro Val Thr Thr Arg Arg Gly Leu Arg Asp  
 20 25 30  
 Ser His Ser Ser Glu Glu Asp Glu Ala Ser Ser Gln Thr Asp Leu Ser  
 35 40 45  
 Gln Thr Ile Ser Lys Lys Thr Val Arg Ser Ile Gln Glu Ala Pro Val  
 50 55 60  
 Ser Glu Asp Leu Val Ile Arg Leu Arg Arg Pro Pro Leu Arg Cys Pro  
 65 70 75 80  
 Arg Tyr Glu Ala Thr Ser Val Gln Gln Lys Val Asn Phe Ser Glu Glu  
 85 90 95  
 Gly Glu Thr Glu Glu Asp Asp Gln Asp Ser Ser His Ser Ser Val Thr  
 100 105 110  
 Thr Val Lys Ala Arg Ser Arg Asp Ser Asp Glu Ser Gly Asp Lys Thr  
 115 120 125  
 Thr Arg Ser Ser Ser Gln Tyr Ile Glu Ser Phe Trp Gln Ser Ser Gln  
 130 135 140  
 Ser Gln Asn Phe Thr Ala His Asp Lys Gln Arg Ser Val Leu Ser Ser  
 145 150 155 160  
 Gly Tyr Gln Lys Thr Pro Gln Glu Trp Ala Pro Gln Thr Ala Arg Ile  
 165 170 175  
 Arg Thr Arg Met Gln Asn Asp Ser Ile Leu Lys Ser Glu Leu Gly Asn  
 180 185 190

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Gln Ser Pro Ser Thr Ser Ser Arg Gln Val Thr Gly Gln Pro Gln Asn  
 195 200 205  
 Ala Ser Phe Val Lys Arg Asn Arg Trp Trp Leu Leu Pro Leu Ile Ala  
 210 215 220  
 Ala Leu Ala Ser Gly Ser Phe Trp Phe Phe Ser Thr Pro Glu Val Glu  
 225 230 235 240  
 Thr Thr Ala Val Gln Glu Phe Gln Asn Gln Met Asn Gln Leu Lys Asn  
 245 250 255  
 Lys Tyr Gln Gly Gln Asp Glu Lys Leu Trp Lys Arg Ser Gln Thr Phe  
 260 265 270  
 Leu Glu Lys His Leu Asn Ser Ser His Pro Arg Ser Gln Pro Ala Ile  
 275 280 285  
 Leu Leu Leu Thr Ala Ala Arg Asp Ala Glu Glu Ala Leu Arg Cys Leu  
 290 295 300  
 Ser Glu Gln Ile Ala Asp Ala Tyr Ser Ser Phe Arg Ser Val Arg Ala  
 305 310 315 320  
 Ile Arg Ile Asp Gly Thr Asp Lys Ala Thr Gln Asp Ser Asp Thr Val  
 325 330 335  
 Lys Leu Glu Val Asp Gln Glu Leu Ser Asn Gly Phe Lys Asn Gly Gln  
 340 345 350  
 Asn Ala Ala Val Val His Arg Phe Glu Ser Phe Pro Ala Gly Ser Thr  
 355 360 365  
 Leu Ile Phe Tyr Lys Tyr Cys Asp His Glu Asn Ala Ala Phe Lys Asp  
 370 375 380  
 Val Ala Leu Val Leu Thr Val Leu Leu Glu Glu Glu Thr Leu Gly Thr  
 385 390 395 400  
 Ser Leu Gly Leu Lys Glu Val Glu Glu Lys Val Arg Asp Phe Leu Lys  
 405 410 415  
 Val Lys Phe Thr Asn Ser Asn Thr Pro Asn Ser Tyr Asn His Met Asp  
 420 425 430  
 Pro Asp Lys Leu Asn Gly Leu Trp Ser Arg Ile Ser His Leu Val Leu  
 435 440 445  
 Pro Val Gln Pro Glu Asn Ala Leu Lys Arg Gly Ile Cys Leu  
 450 455 460

&lt;210&gt; 265

&lt;211&gt; 192

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 265

Met Phe Ser Gln Phe Thr Asp Ile Lys Arg Lys Asp Phe Gly Ile Met  
 1 5 10 15  
 Phe Leu His His Leu Val Ser Ile Phe Leu Ile Thr Phe Ser Tyr Val  
 20 25 30  
 Asn Asn Met Ala Arg Val Gly Thr Leu Val Leu Cys Leu His Asp Ser  
 35 40 45  
 Ala Asp Ala Leu Leu Glu Ala Ala Lys Met Ala Asn Tyr Ala Lys Phe  
 50 55 60  
 Gln Lys Met Cys Asp Leu Leu Phe Val Met Phe Ala Val Val Phe Ile  
 65 70 75 80  
 Thr Thr Arg Leu Gly Ile Phe Pro Leu Trp Val Leu Asn Thr Thr Leu  
 85 90 95  
 Phe Glu Ser Trp Glu Ile Val Gly Pro Tyr Pro Ser Trp Trp Val Phe  
 100 105 110  
 Asn Leu Leu Leu Leu Val Gln Gly Leu Asn Cys Phe Trp Ser Tyr  
 115 120 125



Leu Ile Val Lys Ile Ala Cys Lys Ala Val Ser Arg Gly Lys Val Ser  
 130 135 140  
 Lys Asp Asp Arg Ser Asp Ile Glu Ser Ser Ser Asp Glu Glu Asp Ser  
 145 150 155 160  
 Glu Pro Pro Gly Lys Asn Pro His Thr Ala Thr Thr Thr Asn Gly Thr  
 165 170 175  
 Ser Gly Thr Asn Gly Tyr Leu Leu Thr Gly Ser Cys Ser Met Asp Asp  
 180 185 190

&lt;210&gt; 266

&lt;211&gt; 1838

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 266

Met Asp Val His Thr Arg Trp Lys Ala Arg Ser Ala Leu Arg Pro Gly  
 1 5 10 15  
 Ala Pro Leu Leu Pro Pro Leu Leu Leu Leu Trp Ala Pro Pro  
 20 25 30  
 Pro Ser Arg Ala Ala Gln Pro Ala Asp Leu Leu Lys Val Leu Asp Phe  
 35 40 45  
 His Asn Leu Pro Asp Gly Ile Thr Lys Thr Thr Gly Phe Cys Ala Thr  
 50 55 60  
 Arg Arg Ser Ser Lys Gly Pro Asp Val Ala Tyr Arg Val Thr Lys Asp  
 65 70 75 80  
 Ala Gln Leu Ser Ala Pro Thr Lys Gln Leu Tyr Pro Ala Ser Ala Phe  
 85 90 95  
 Pro Glu Asp Phe Ser Ile Leu Thr Thr Val Lys Ala Lys Lys Gly Ser  
 100 105 110  
 Gln Ala Phe Leu Val Ser Ile Tyr Asn Glu Gln Gly Ile Gln Gln Ile  
 115 120 125  
 Gly Leu Glu Leu Gly Arg Ser Pro Val Phe Leu Tyr Glu Asp His Thr  
 130 135 140  
 Gly Lys Pro Gly Pro Glu Asp Tyr Pro Leu Phe Arg Gly Ile Asn Leu  
 145 150 155 160  
 Ser Asp Gly Lys Trp His Arg Ile Ala Leu Ser Val His Lys Lys Asn  
 165 170 175  
 Val Thr Leu Ile Leu Asp Cys Lys Lys Lys Thr Thr Lys Phe Leu Asp  
 180 185 190  
 Arg Ser Asp His Pro Met Ile Asp Ile Asn Gly Ile Ile Val Phe Gly  
 195 200 205  
 Thr Arg Ile Leu Asp Glu Glu Val Phe Glu Gly Asp Ile Gln Gln Leu  
 210 215 220  
 Leu Phe Val Ser Asp His Arg Ala Ala Tyr Asp Tyr Cys Glu His Tyr  
 225 230 235 240  
 Ser Pro Asp Cys Asp Thr Ala Val Pro Asp Thr Pro Gln Ser Gln Asp  
 245 250 255  
 Pro Asn Pro Asp Glu Tyr Tyr Thr Glu Gly Asp Gly Glu Gly Thr  
 260 265 270  
 Tyr Tyr Tyr Glu Tyr Pro Tyr Tyr Glu Asp Pro Glu Asp Leu Gly Lys  
 275 280 285  
 Glu Pro Thr Pro Ser Lys Lys Pro Val Glu Ala Ala Lys Glu Thr Thr  
 290 295 300  
 Glu Val Pro Glu Glu Leu Thr Pro Thr Pro Thr Glu Ala Ala Pro Met  
 305 310 315 320  
 Pro Glu Thr Ser Glu Gly Ala Gly Lys Glu Glu Asp Val Gly Ile Gly  
 325 330 335

Asp Tyr Asp Tyr Val Pro Ser Glu Asp Tyr Tyr Thr Pro Ser Pro Tyr  
 340 345 350  
 Asp Asp Leu Thr Tyr Gly Glu Gly Glu Glu Asn Pro Asp Gln Pro Thr  
 355 360 365  
 Asp Pro Gly Ala Gly Ala Glu Ile Pro Thr Ser Thr Ala Asp Thr Ser  
 370 375 380  
 Asn Ser Ser Asn Pro Ala Pro Pro Pro Gly Glu Gly Ala Asp Asp Leu  
 385 390 395  
 Glu Gly Glu Phe Thr Glu Glu Thr Ile Arg Asn Leu Asp Glu Asn Tyr  
 405 410 415  
 Tyr Asp Pro Tyr Tyr Asp Pro Thr Ser Ser Pro Ser Glu Ile Gly Pro  
 420 425 430  
 Gly Met Pro Ala Asn Gln Asp Thr Ile Tyr Glu Gly Ile Gly Gly Pro  
 435 440 445  
 Arg Gly Glu Lys Gly Gln Lys Gly Glu Pro Ala Ile Ile Glu Pro Gly  
 450 455 460  
 Met Leu Ile Glu Gly Pro Pro Gly Pro Glu Gly Pro Ala Gly Leu Pro  
 465 470 475  
 Gly Pro Pro Gly Thr Met Gly Pro Thr Gly Gln Val Gly Asp Pro Gly  
 485 490 495  
 Glu Arg Gly Pro Pro Gly Arg Pro Gly Leu Pro Gly Ala Asp Gly Leu  
 500 505 510  
 Pro Gly Pro Pro Gly Thr Met Leu Met Leu Pro Phe Arg Phe Gly Gly  
 515 520 525  
 Gly Gly Asp Ala Gly Ser Lys Gly Pro Met Val Ser Ala Gln Glu Ser  
 530 535 540  
 Gln Ala Gln Ala Ile Leu Gln Gln Ala Arg Leu Ala Leu Arg Gly Pro  
 545 550 555  
 Ala Gly Pro Met Gly Leu Thr Gly Arg Pro Gly Pro Val Gly Pro Pro  
 565 570 575  
 Gly Ser Gly Gly Leu Lys Gly Glu Pro Gly Asp Val Gly Pro Gln Gly  
 580 585 590  
 Pro Arg Gly Val Gln Gly Pro Pro Gly Pro Ala Gly Lys Pro Gly Arg  
 595 600 605  
 Arg Gly Arg Ala Gly Ser Asp Gly Ala Arg Gly Met Pro Gly Gln Thr  
 610 615 620  
 Gly Pro Lys Gly Asp Arg Gly Phe Asp Gly Leu Ala Gly Leu Pro Gly  
 625 630 635  
 Glu Lys Gly His Arg Gly Asp Pro Gly Pro Ser Gly Pro Pro Gly Pro  
 645 650 655  
 Pro Gly Asp Asp Gly Glu Arg Gly Asp Asp Gly Glu Val Gly Pro Arg  
 660 665 670  
 Gly Leu Pro Gly Glu Pro Gly Pro Arg Gly Leu Leu Gly Pro Lys Gly  
 675 680 685  
 Pro Pro Gly Pro Pro Gly Pro Pro Gly Val Thr Gly Met Asp Gly Gln  
 690 695 700  
 Pro Gly Pro Lys Gly Asn Val Gly Pro Gln Gly Glu Pro Gly Pro Pro  
 705 710 715  
 Gly Gln Gln Gly Asn Pro Gly Ala Gln Gly Leu Pro Gly Pro Gln Gly  
 725 730 735  
 Ala Ile Gly Pro Pro Gly Glu Lys Gly Pro Leu Gly Lys Pro Gly Leu  
 740 745 750  
 Pro Gly Met Pro Gly Ala Asp Gly Pro Pro Gly His Pro Gly Lys Glu  
 755 760 765  
 Gly Pro Pro Gly Glu Lys Gly Gly Gln Gly Pro Pro Gly Pro Gln Gly  
 770 775 780  
 Pro Ile Gly Tyr Pro Gly Pro Arg Gly Val Lys Gly Ala Asp Gly Ile  
 785 790 795  
 Arg Gly Leu Lys Gly Thr Lys Gly Glu Lys Gly Glu Asp Gly Phe Pro  
 805 810 815  
 Gly Phe Lys Gly Asp Met Gly Ile Lys Gly Asp Arg Gly Glu Ile Gly  
 820 825 830

Pro Pro Gly Pro Arg Gly Glu Asp Gly Pro Glu Gly Pro Lys Gly Arg  
 835 840 845  
 Gly Gly Pro Asn Gly Asp Pro Gly Pro Leu Gly Pro Pro Gly Glu Lys  
 850 855 860  
 Gly Lys Leu Gly Val Pro Gly Leu Pro Gly Tyr Pro Gly Arg Gln Gly  
 865 870 875 880  
 Pro Lys Gly Ser Ile Gly Phe Pro Gly Phe Pro Gly Ala Asn Gly Glu  
 885 890 895  
 Lys Gly Gly Arg Gly Thr Pro Gly Lys Pro Gly Pro Arg Gly Gln Arg  
 900 905 910  
 Gly Pro Thr Gly Pro Arg Gly Glu Arg Gly Pro Arg Gly Ile Thr Gly  
 915 920 925  
 Lys Pro Gly Pro Lys Gly Asn Ser Gly Gly Asp Gly Pro Ala Gly Pro  
 930 935 940  
 Pro Gly Glu Arg Gly Pro Asn Gly Pro Gln Gly Pro Thr Gly Phe Pro  
 945 950 955 960  
 Gly Pro Lys Gly Pro Pro Gly Pro Pro Gly Lys Asp Gly Leu Pro Gly  
 965 970 975  
 His Pro Gly Gln Arg Gly Glu Thr Gly Phe Gln Gly Lys Thr Gly Pro  
 980 985 990  
 Pro Gly Pro Pro Gly Val Val Gly Pro Gln Gly Pro Thr Gly Glu Thr  
 995 1000 1005  
 Gly Pro Met Gly Glu Arg Gly His Pro Gly Pro Pro Gly Pro Pro  
 1010 1015 1020  
 Gly Glu Gln Gly Leu Pro Gly Leu Ala Gly Lys Glu Gly Thr Lys  
 1025 1030 1035  
 Gly Asp Pro Gly Pro Ala Gly Leu Pro Gly Lys Asp Gly Pro Pro  
 1040 1045 1050  
 Gly Leu Arg Gly Phe Pro Gly Asp Arg Gly Leu Pro Gly Pro Val  
 1055 1060 1065  
 Gly Ala Leu Gly Leu Lys Gly Asn Glu Gly Pro Pro Gly Pro Pro  
 1070 1075 1080  
 Gly Pro Ala Gly Ser Pro Gly Glu Arg Gly Pro Ala Gly Ala Ala  
 1085 1090 1095  
 Gly Pro Ile Gly Ile Pro Gly Arg Pro Gly Pro Gln Gly Pro Pro  
 1100 1105 1110  
 Gly Pro Ala Gly Glu Lys Gly Ala Pro Gly Glu Lys Gly Pro Gln  
 1115 1120 1125  
 Gly Pro Ala Gly Arg Asp Gly Leu Gln Gly Pro Val Gly Leu Pro  
 1130 1135 1140  
 Gly Pro Ala Gly Pro Val Gly Pro Pro Gly Glu Asp Gly Asp Lys  
 1145 1150 1155  
 Gly Glu Ile Gly Glu Pro Gly Gln Lys Gly Ser Lys Gly Asp Lys  
 1160 1165 1170  
 Gly Glu Gln Gly Pro Pro Gly Pro Thr Gly Pro Gln Gly Pro Ile  
 1175 1180 1185  
 Gly Gln Pro Gly Pro Ser Gly Ala Asp Gly Glu Pro Gly Pro Arg  
 1190 1195 1200  
 Gly Gln Gln Gly Leu Phe Gly Gln Lys Gly Asp Glu Gly Pro Arg  
 1205 1210 1215  
 Gly Phe Pro Gly Pro Pro Gly Pro Val Gly Leu Gln Gly Leu Pro  
 1220 1225 1230  
 Gly Pro Pro Gly Glu Lys Gly Glu Thr Gly Asp Val Gly Gln Met  
 1235 1240 1245  
 Gly Pro Pro Gly Pro Pro Gly Pro Arg Gly Pro Ser Gly Ala Pro  
 1250 1255 1260  
 Gly Ala Asp Gly Pro Gln Gly Pro Pro Gly Gly Ile Gly Asn Pro  
 1265 1270 1275  
 Gly Ala Val Gly Glu Lys Gly Glu Pro Gly Glu Ala Gly Glu Pro  
 1280 1285 1290  
 Gly Pro Ser Gly Arg Ser Gly Pro Pro Gly Pro Lys Gly Glu Arg  
 1295 1300 1305

Gly	Glu	Lys	Gly	Glu	Ser	Gly	Pro	Ser	Gly	Ala	Ala	Gly	Pro	Pro
1310						1315					1320			
Gly	Pro	Lys	Gly	Pro	Pro	Gly	Asp	Asp	Gly	Pro	Lys	Gly	Ser	Pro
1325						1330					1335			
Gly	Pro	Val	Gly	Phe	Pro	Gly	Asp	Pro	Gly	Pro	Pro	Gly	Glu	Pro
1340						1345					1350			
Gly	Pro	Ala	Gly	Gln	Asp	Gly	Pro	Pro	Gly	Asp	Lys	Gly	Asp	Asp
1355						1360					1365			
Gly	Glu	Pro	Gly	Gln	Thr	Gly	Ser	Pro	Gly	Pro	Thr	Gly	Glu	Pro
1370						1375					1380			
Gly	Pro	Ser	Gly	Pro	Pro	Gly	Lys	Arg	Gly	Pro	Pro	Gly	Pro	Ala
1385						1390					1395			
Gly	Pro	Glu	Gly	Arg	Gln	Gly	Glu	Lys	Gly	Ala	Lys	Gly	Glu	Ala
1400						1405					1410			
Gly	Leu	Glu	Gly	Pro	Pro	Gly	Lys	Thr	Gly	Pro	Ile	Gly	Pro	Gln
1415						1420					1425			
Gly	Ala	Pro	Gly	Lys	Pro	Gly	Pro	Asp	Gly	Leu	Arg	Gly	Ile	Pro
1430						1435					1440			
Gly	Pro	Val	Gly	Glu	Gln	Gly	Leu	Pro	Gly	Ser	Pro	Gly	Pro	Asp
1445						1450					1455			
Gly	Pro	Pro	Gly	Pro	Met	Gly	Pro	Pro	Gly	Leu	Pro	Gly	Leu	Lys
1460						1465					1470			
Gly	Asp	Ser	Gly	Pro	Lys	Gly	Glu	Lys	Gly	His	Pro	Gly	Leu	Ile
1475						1480					1485			
Gly	Leu	Ile	Gly	Pro	Pro	Gly	Glu	Gln	Gly	Glu	Lys	Gly	Asp	Arg
1490						1495					1500			
Gly	Leu	Pro	Gly	Pro	Gln	Gly	Ser	Ser	Gly	Pro	Lys	Gly	Glu	Gln
1505						1510					1515			
Gly	Ile	Thr	Gly	Pro	Ser	Gly	Pro	Ile	Gly	Pro	Pro	Gly	Pro	Pro
1520						1525					1530			
Gly	Leu	Pro	Gly	Pro	Pro	Gly	Pro	Lys	Gly	Ala	Lys	Gly	Ser	Ser
1535						1540					1545			
Gly	Pro	Thr	Gly	Pro	Lys	Gly	Glu	Ala	Gly	His	Pro	Gly	Pro	Pro
1550						1555					1560			
Gly	Pro	Pro	Gly	Pro	Pro	Gly	Glu	Val	Ile	Gln	Pro	Leu	Pro	Ile
1565						1570					1575			
Gln	Ala	Ser	Arg	Thr	Arg	Arg	Asn	Ile	Asp	Ala	Ser	Gln	Leu	Leu
1580						1585					1590			
Asp	Asp	Gly	Asn	Gly	Glu	Asn	Tyr	Val	Asp	Tyr	Ala	Asp	Gly	Met
1595						1600					1605			
Glu	Glu	Ile	Phe	Gly	Ser	Leu	Asn	Ser	Leu	Lys	Leu	Glu	Ile	Glu
1610						1615					1620			
Gln	Met	Lys	Arg	Pro	Leu	Gly	Thr	Gln	Gln	Asn	Pro	Ala	Arg	Thr
1625						1630					1635			
Cys	Lys	Asp	Leu	Gln	Leu	Cys	His	Pro	Asp	Phe	Pro	Asp	Gly	Glu
1640						1645					1650			
Tyr	Trp	Val	Asp	Pro	Asn	Gln	Gly	Cys	Ser	Arg	Asp	Ser	Phe	Lys
1655						1660					1665			
Val	Tyr	Cys	Asn	Phe	Thr	Ala	Gly	Gly	Ser	Thr	Cys	Val	Phe	Pro
1670						1675					1680			
Asp	Lys	Lys	Ser	Glu	Gly	Ala	Arg	Ile	Thr	Ser	Trp	Pro	Lys	Glu
1685						1690					1695			
Asn	Pro	Gly	Ser	Trp	Phe	Ser	Glu	Phe	Lys	Arg	Gly	Lys	Leu	Leu
1700						1705					1710			
Ser	Tyr	Val	Asp	Ala	Glu	Gly	Asn	Pro	Val	Gly	Val	Val	Gln	Met
1715						1720					1725			
Thr	Phe	Leu	Arg	Leu	Leu	Ser	Ala	Ser	Ala	His	Gln	Asn	Val	Thr
1730						1735					1740			
Tyr	His	Cys	Tyr	Gln	Ser	Val	Ala	Trp	Gln	Asp	Ala	Ala	Thr	Gly
1745						1750					1755			
Ser	Tyr	Asp	Lys	Ala	Leu	Arg	Phe	Leu	Gly	Ser	Asn	Asp	Glu	Glu
1760						1765					1770			

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Met Ser Tyr Asp Asn Asn Pro Tyr Ile Arg Ala Leu Val Asp Gly  
 1775 1780 1785  
 Cys Ala Thr Lys Lys Gly Tyr Gln Lys Thr Val Leu Glu Ile Asp  
 1790 1795 1800  
 Thr Pro Lys Val Glu Gln Val Pro Ile Val Asp Ile Met Phe Asn  
 1805 1810 1815  
 Asp Phe Gly Glu Ala Ser Gln Lys Phe Gly Phe Glu Val Gly Pro  
 1820 1825 1830  
 Ala Cys Phe Met Gly  
 1835

&lt;210&gt; 267

&lt;211&gt; 109

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 267

Met Lys Phe Ile Ser Thr Ser Leu Leu Leu Met Leu Leu Val Ser Ser  
 1 5 10 15  
 Leu Ser Pro Val Gln Gly Val Leu Glu Val Tyr Tyr Thr Ser Leu Arg  
 20 25 30  
 Cys Arg Cys Val Gln Glu Ser Ser Val Phe Ile Pro Arg Arg Phe Ile  
 35 40 45  
 Asp Arg Ile Gln Ile Leu Pro Arg Gly Asn Gly Cys Pro Arg Lys Glu  
 50 55 60  
 Ile Ile Val Trp Lys Lys Asn Lys Ser Ile Val Cys Val Asp Pro Gln  
 65 70 75 80  
 Ala Glu Trp Ile Gln Arg Met Met Glu Val Leu Arg Lys Arg Ser Ser  
 85 90 95  
 Ser Thr Leu Pro Val Pro Val Phe Lys Arg Lys Ile Pro  
 100 105

&lt;210&gt; 268

&lt;211&gt; 504

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 268

Met Phe Pro Arg Glu Lys Thr Trp Asn Ile Ser Phe Ala Gly Cys Gly  
 1 5 10 15  
 Phe Leu Gly Val Tyr Tyr Val Gly Val Ala Ser Cys Leu Arg Glu His  
 20 25 30  
 Ala Pro Phe Leu Val Ala Asn Ala Thr His Ile Tyr Gly Ala Ser Ala  
 35 40 45  
 Gly Ala Leu Thr Ala Thr Ala Leu Val Thr Gly Val Cys Leu Gly Glu  
 50 55 60  
 Ala Gly Ala Lys Phe Ile Glu Val Ser Lys Glu Ala Arg Lys Arg Phe  
 65 70 75 80  
 Leu Gly Pro Leu His Pro Ser Phe Asn Leu Val Lys Ile Ile Arg Ser  
 85 90 95  
 Phe Leu Leu Lys Val Leu Pro Ala Asp Ser His Glu His Ala Ser Gly  
 100 105 110

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Arg Leu Gly Ile Ser Leu Thr Arg Val Ser Asp Gly Glu Asn Val Ile  
 115 120 125  
 Ile Ser His Phe Asn Ser Lys Asp Glu Leu Ile Gln Ala Asn Val Cys  
 130 135 140  
 Ser Gly Phe Ile Pro Val Tyr Cys Gly Leu Ile Pro Pro Ser Leu Gln  
 145 150 155 160  
 Gly Val Arg Tyr Val Asp Gly Gly Ile Ser Asp Asn Leu Pro Leu Tyr  
 165 170 175  
 Glu Leu Lys Asn Thr Ile Thr Val Ser Pro Phe Ser Gly Glu Ser Asp  
 180 185 190  
 Ile Cys Pro Gln Asp Ser Ser Thr Asn Ile His Glu Leu Arg Val Thr  
 195 200 205  
 Asn Thr Ser Ile Gln Phe Asn Leu Arg Asn Leu Tyr Arg Leu Ser Lys  
 210 215 220  
 Ala Leu Phe Pro Pro Glu Pro Leu Val Leu Arg Glu Met Cys Lys Gln  
 225 230 235 240  
 Gly Tyr Arg Asp Gly Leu Arg Phe Leu Gln Arg Asn Gly Leu Leu Asn  
 245 250 255  
 Arg Pro Asn Pro Leu Leu Ala Leu Pro Pro Ala Arg Pro His Gly Pro  
 260 265 270  
 Glu Asp Lys Asp Gln Ala Val Glu Ser Ala Gln Ala Glu Asp Tyr Ser  
 275 280 285  
 Gln Leu Pro Gly Glu Asp His Ile Leu Glu His Leu Pro Ala Arg Leu  
 290 295 300  
 Asn Glu Ala Leu Leu Glu Ala Cys Val Glu Pro Thr Asp Leu Leu Thr  
 305 310 315 320  
 Thr Leu Ser Asn Met Leu Pro Val Arg Leu Ala Thr Ala Met Met Val  
 325 330 335  
 Pro Tyr Thr Leu Pro Leu Glu Ser Ala Leu Ser Phe Thr Ile Arg Leu  
 340 345 350  
 Leu Glu Trp Leu Pro Asp Val Pro Glu Asp Ile Arg Trp Met Lys Glu  
 355 360 365  
 Gln Thr Gly Ser Ile Cys Gln Tyr Leu Val Met Arg Ala Lys Arg Lys  
 370 375 380  
 Leu Gly Arg His Leu Pro Ser Arg Leu Pro Glu Gln Val Glu Leu Arg  
 385 390 395 400  
 Arg Val Gln Ser Leu Pro Ser Val Pro Leu Ser Cys Ala Ala Tyr Arg  
 405 410 415  
 Glu Ala Leu Pro Gly Trp Met Arg Asn Asn Leu Ser Leu Gly Asp Ala  
 420 425 430  
 Leu Ala Lys Trp Glu Glu Cys Gln Arg Gln Leu Leu Leu Gly Leu Phe  
 435 440 445  
 Cys Thr Asn Val Ala Phe Pro Pro Glu Ala Leu Arg Met Arg Ala Pro  
 450 455 460  
 Ala Asp Pro Ala Pro Ala Pro Ala Asp Pro Ala Ser Pro Gln His Gln  
 465 470 475 480  
 Pro Ala Gly Pro Ala Pro Leu Leu Ser Thr Pro Ala Pro Glu Ala Arg  
 485 490 495  
 Pro Val Ile Gly Ala Leu Gly Leu  
 500

&lt;210&gt; 269

&lt;211&gt; 1498

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 269  
 Met Val Ala Leu Arg Gly Leu Gly Ser Gly Leu Gln Pro Trp Cys Pro  
 1 5 10 15  
 Leu Asp Leu Arg Leu Glu Trp Val Asp Thr Val Trp Glu Leu Asp Phe  
 20 25 30  
 Thr Glu Thr Glu Pro Leu Asp Pro Ser Ile Glu Ala Glu Ile Ile Glu  
 35 40 45  
 Thr Gly Leu Ala Ala Phe Thr Lys Leu Tyr Glu Ser Leu Leu Pro Phe  
 50 55 60  
 Ala Thr Gly Glu His Gly Ser Met Glu Ser Ile Trp Thr Phe Phe Ile  
 65 70 75 80  
 Glu Asn Asn Val Ser His Ser Thr Leu Val Ala Leu Phe Tyr His Phe  
 85 90 95  
 Val Gln Ile Val His Lys Lys Asn Val Ser Val Gln Tyr Arg Glu Tyr  
 100 105 110  
 Gly Leu His Ala Ala Gly Leu Tyr Phe Leu Leu Leu Glu Val Pro Gly  
 115 120 125  
 Ser Val Ala Asn Gln Val Phe His Pro Val Met Phe Asp Lys Cys Ile  
 130 135 140  
 Gln Thr Leu Lys Lys Ser Trp Pro Gln Glu Ser Asn Leu Asn Arg Lys  
 145 150 155 160  
 Arg Lys Lys Glu Gln Pro Lys Ser Ser Gln Ala Asn Pro Gly Arg His  
 165 170 175  
 Arg Lys Arg Gly Lys Pro Pro Arg Arg Glu Asp Ile Glu Met Asp Glu  
 180 185 190  
 Ile Ile Glu Glu Gln Glu Asp Glu Asn Ile Cys Phe Ser Ala Arg Asp  
 195 200 205  
 Leu Ser Gln Ile Arg Asn Ala Ile Phe His Leu Leu Lys Asn Phe Leu  
 210 215 220  
 Arg Leu Leu Pro Lys Phe Ser Leu Lys Glu Lys Pro Gln Cys Val Gln  
 225 230 235 240  
 Asn Cys Ile Glu Val Phe Val Ser Leu Thr Asn Phe Glu Pro Val Leu  
 245 250 255  
 His Glu Cys His Val Thr Gln Ala Arg Ala Leu Asn Gln Ala Lys Tyr  
 260 265 270  
 Ile Pro Glu Leu Ala Tyr Tyr Gly Leu Tyr Leu Leu Cys Ser Pro Ile  
 275 280 285  
 His Gly Glu Gly Asp Lys Val Ile Ser Cys Val Phe His Gln Met Leu  
 290 295 300  
 Ser Val Ile Leu Met Leu Glu Val Gly Glu Gly Ser His Arg Ala Pro  
 305 310 315 320  
 Leu Ala Val Thr Ser Gln Val Ile Asn Cys Arg Asn Gln Ala Val Gln  
 325 330 335  
 Phe Ile Ser Ala Leu Val Asp Glu Leu Lys Glu Ser Ile Phe Pro Val  
 340 345 350  
 Val Arg Ile Leu Leu Gln His Ile Cys Ala Lys Val Val Asp Lys Ser  
 355 360 365  
 Glu Tyr Arg Thr Phe Ala Ala Gln Ser Leu Val Gln Leu Leu Ser Lys  
 370 375 380  
 Leu Pro Cys Gly Glu Tyr Ala Met Phe Ile Ala Trp Leu Tyr Lys Tyr  
 385 390 395 400  
 Ser Arg Ser Ser Lys Ile Pro His Arg Val Phe Thr Leu Asp Val Val  
 405 410 415  
 Leu Ala Leu Leu Glu Leu Pro Glu Arg Glu Val Asp Asn Thr Leu Ser  
 420 425 430  
 Leu Glu His Gln Lys Phe Leu Lys His Lys Phe Leu Val Gln Glu Ile  
 435 440 445  
 Met Phe Asp Arg Cys Leu Asp Lys Ala Pro Thr Val Arg Ser Lys Ala  
 450 455 460  
 Leu Ser Ser Phe Ala His Cys Leu Glu Leu Thr Val Thr Ser Ala Ser  
 465 470 475 480

Glu	Ser	Ile	Leu	Glu	Leu	Leu	Ile	Asn	Ser	Pro	Thr	Phe	Ser	Val	Ile		
				485					490					495			
Glu	Ser	His	Pro	Gly	Thr	Leu	Leu	Arg	Asn	Ser	Ser	Ala	Phe	Ser	Tyr		
			500					505					510				
Gln	Arg	Gln	Thr	Ser	Asn	Arg	Ser	Glu	Pro	Ser	Gly	Glu	Ile	Asn	Ile		
		515					520					525					
Asp	Ser	Ser	Gly	Glu	Thr	Val	Gly	Ser	Gly	Glu	Arg	Cys	Val	Met	Ala		
	530				535						540						
Met	Leu	Arg	Arg	Arg	Ile	Arg	Asp	Glu	Lys	Thr	Asn	Val	Arg	Lys	Ser		
545					550					555					560		
Ala	Leu	Gln	Val	Leu	Val	Ser	Ile	Leu	Lys	His	Cys	Asp	Val	Ser	Gly		
			565						570					575			
Met	Lys	Glu	Asp	Leu	Trp	Ile	Leu	Gln	Asp	Gln	Cys	Arg	Asp	Pro	Ala		
			580					585					590				
Val	Ser	Val	Arg	Lys	Gln	Ala	Leu	Gln	Ser	Leu	Thr	Glu	Leu	Leu	Met		
		595					600					605					
Ala	Gln	Pro	Arg	Cys	Val	Gln	Ile	Gln	Lys	Ala	Trp	Leu	Arg	Gly	Val		
	610				615						620						
Val	Pro	Val	Val	Met	Asp	Cys	Glu	Ser	Thr	Val	Gln	Glu	Lys	Ala	Leu		
625				630					635						640		
Glu	Phe	Leu	Asp	Gln	Leu	Leu	Leu	Gln	Asn	Ile	Arg	His	His	Ser	His		
			645					650						655			
Phe	His	Ser	Gly	Asp	Asp	Ser	Gln	Val	Leu	Ala	Trp	Ala	Leu	Leu	Thr		
			660				665						670				
Leu	Leu	Thr	Thr	Glu	Ser	Gln	Glu	Leu	Ser	Arg	Tyr	Leu	Asn	Lys	Ala		
		675					680					685					
Phe	His	Ile	Trp	Ser	Lys	Lys	Glu	Lys	Phe	Ser	Pro	Thr	Phe	Ile	Asn		
	690				695						700						
Asn	Val	Ile	Ser	His	Thr	Gly	Thr	Glu	His	Ser	Ala	Pro	Ala	Trp	Met		
705				710					715						720		
Leu	Leu	Ser	Lys	Ile	Ala	Gly	Ser	Ser	Pro	Arg	Leu	Asp	Tyr	Ser	Arg		
			725					730						735			
Ile	Ile	Gln	Ser	Trp	Glu	Lys	Ile	Ser	Ser	Gln	Gln	Asn	Pro	Asn	Ser		
		740					745						750				
Asn	Thr	Leu	Gly	His	Ile	Leu	Cys	Val	Ile	Gly	His	Ile	Ala	Lys	His		
	755						760					765					
Leu	Pro	Lys	Ser	Thr	Arg	Asp	Lys	Val	Thr	Asp	Ala	Val	Lys	Cys	Lys		
	770				775						780						
Leu	Asn	Gly	Phe	Gln	Trp	Ser	Leu	Glu	Val	Ile	Ser	Ser	Ala	Val	Asp		
785				790					795						800		
Ala	Leu	Gln	Arg	Leu	Cys	Arg	Ala	Ser	Ala	Glu	Thr	Pro	Ala	Glu	Glu		
			805				810							815			
Gln	Glu	Leu	Leu	Thr	Gln	Val	Cys	Gly	Asp	Val	Leu	Ser	Thr	Cys	Glu		
		820					825						830				
His	Arg	Leu	Ser	Asn	Ile	Val	Leu	Lys	Glu	Asn	Gly	Thr	Gly	Asn	Met		
	835						840					845					
Asp	Glu	Asp	Leu	Leu	Val	Lys	Tyr	Ile	Phe	Thr	Leu	Gly	Asp	Ile	Ala		
	850				855						860						
Gln	Leu	Cys	Pro	Ala	Arg	Val	Glu	Lys	Arg	Ile	Phe	Leu	Leu	Ile	Gln		
865				870					875						880		
Ser	Val	Leu	Ala	Ser	Ser	Ala	Asp	Ala	Asp	His	Ser	Pro	Ser	Ser	Gln		
			885				890							895			
Gly	Ser	Ser	Glu	Ala	Pro	Ala	Ser	Gln	Pro	Pro	Pro	Gln	Val	Arg	Gly		
		900					905						910				
Ser	Val	Met	Pro	Ser	Val	Ile	Arg	Ala	His	Ala	Ile	Ile	Thr	Leu	Gly		
		915					920					925					
Lys	Leu	Cys	Leu	Gln	His	Glu	Asp	Leu	Ala	Lys	Lys	Ser	Ile	Pro	Ala		
	930				935						940						
Leu	Val	Arg	Glu	Leu	Glu	Val	Cys	Glu	Asp	Val	Ala	Val	Arg	Asn	Asn		
945				950					955					960			
Val	Ile	Ile	Val	Met	Cys	Asp	Leu	Cys	Ile	Arg	Tyr	Thr	Ile	Met	Val		
			965						970					975			



Asp	Lys	Tyr	Ile	Pro	Asn	Ile	Ser	Met	Cys	Leu	Lys	Asp	Ser	Asp	Pro
			980					985						990	
Phe	Ile	Arg	Lys	Gln	Thr	Leu	Ile	Leu	Leu	Thr	Asn	Leu	Leu	Gln	Glu
		995					1000					1005			
Glu	Phe	Val	Lys	Trp	Lys	Gly	Ser	Leu	Phe	Phe	Arg	Phe	Val	Ser	
	1010					1015					1020				
Thr	Leu	Ile	Asp	Ser	His	Pro	Asp	Ile	Ala	Ser	Phe	Gly	Glu	Phe	
	1025					1030					1035				
Cys	Leu	Ala	His	Leu	Leu	Leu	Lys	Arg	Asn	Pro	Val	Met	Phe	Phe	
	1040					1045					1050				
Gln	His	Phe	Ile	Glu	Cys	Ile	Phe	His	Phe	Asn	Asn	Tyr	Glu	Lys	
	1055					1060					1065				
His	Glu	Lys	Tyr	Asn	Lys	Phe	Pro	Gln	Ser	Glu	Arg	Glu	Lys	Arg	
	1070					1075					1080				
Leu	Phe	Ser	Leu	Lys	Gly	Lys	Ser	Asn	Lys	Glu	Arg	Arg	Met	Lys	
	1085					1090					1095				
Ile	Tyr	Lys	Phe	Leu	Leu	Glu	His	Phe	Thr	Asp	Glu	Gln	Arg	Phe	
	1100					1105					1110				
Asn	Ile	Thr	Ser	Lys	Ile	Cys	Leu	Ser	Ile	Leu	Ala	Cys	Phe	Ala	
	1115					1120					1125				
Asp	Gly	Ile	Leu	Pro	Leu	Asp	Leu	Asp	Ala	Ser	Glu	Leu	Leu	Ser	
	1130					1135					1140				
Asp	Thr	Phe	Glu	Val	Leu	Ser	Ser	Lys	Glu	Ile	Lys	Leu	Leu	Ala	
	1145					1150					1155				
Met	Arg	Ser	Lys	Pro	Asp	Lys	Asp	Leu	Leu	Met	Glu	Glu	Asp	Asp	
	1160					1165					1170				
Met	Ala	Leu	Ala	Asn	Val	Val	Met	Gln	Glu	Ala	Gln	Lys	Lys	Leu	
	1175					1180					1185				
Ile	Ser	Gln	Val	Gln	Lys	Arg	Asn	Phe	Ile	Glu	Asn	Ile	Ile	Pro	
	1190					1195					1200				
Ile	Ile	Ile	Ser	Leu	Lys	Thr	Val	Leu	Glu	Lys	Asn	Lys	Ile	Pro	
	1205					1210					1215				
Ala	Leu	Arg	Glu	Leu	Met	His	Tyr	Leu	Arg	Glu	Val	Met	Gln	Asp	
	1220					1225					1230				
Tyr	Arg	Asp	Glu	Leu	Lys	Asp	Phe	Phe	Ala	Val	Asp	Lys	Gln	Leu	
	1235					1240					1245				
Ala	Ser	Glu	Leu	Glu	Tyr	Asp	Met	Lys	Lys	Tyr	Gln	Glu	Gln	Leu	
	1250					1255					1260				
Val	Gln	Glu	Gln	Glu	Leu	Ala	Lys	His	Ala	Asp	Val	Ala	Gly	Thr	
	1265					1270					1275				
Ala	Gly	Gly	Ala	Glu	Val	Ala	Pro	Val	Ala	Gln	Val	Ala	Leu	Cys	
	1280					1285					1290				
Leu	Glu	Thr	Val	Pro	Val	Pro	Ala	Gly	Gln	Glu	Asn	Pro	Ala	Met	
	1295					1300					1305				
Ser	Pro	Ala	Val	Ser	Gln	Pro	Cys	Thr	Pro	Arg	Ala	Ser	Ala	Gly	
	1310					1315					1320				
His	Val	Ala	Val	Ser	Ser	Pro	Thr	Pro	Glu	Thr	Gly	Pro	Leu	Gln	
	1325					1330					1335				
Arg	Leu	Leu	Pro	Lys	Ala	Arg	Pro	Met	Ser	Leu	Ser	Thr	Ile	Ala	
	1340					1345					1350				
Ile	Leu	Asn	Ser	Val	Lys	Lys	Ala	Val	Glu	Ser	Lys	Ser	Arg	His	
	1355					1360					1365				
Arg	Ser	Arg	Ser	Leu	Gly	Val	Leu	Pro	Phe	Thr	Leu	Asn	Ser	Gly	
	1370					1375					1380				
Ser	Pro	Glu	Lys	Thr	Cys	Ser	Gln	Val	Ser	Ser	Tyr	Ser	Leu	Glu	
	1385					1390					1395				
Gln	Glu	Ser	Asn	Gly	Glu	Ile	Glu	His	Val	Thr	Lys	Arg	Ala	Ile	
	1400					1405					1410				
Ser	Thr	Pro	Glu	Lys	Ser	Ile	Ser	Asp	Val	Thr	Phe	Gly	Ala	Gly	
	1415					1420					1425				
Val	Ser	Tyr	Ile	Gly	Thr	Pro	Arg	Thr	Pro	Ser	Ser	Ala	Lys	Glu	
	1430					1435					1440				

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Lys Ile Glu Gly Arg Ser Gln Gly Asn Asp Ile Leu Cys Leu Ser  
 1445 1450 1455  
 Leu Pro Asp Lys Pro Pro Pro Gln Pro Gln Gln Trp Asn Val Arg  
 1460 1465 1470  
 Ser Pro Ala Arg Asn Lys Asp Thr Pro Ala Cys Ser Arg Arg Ser  
 1475 1480 1485  
 Leu Arg Lys Thr Pro Leu Lys Thr Ala Asn  
 1490 1495

&lt;210&gt; 270

&lt;211&gt; 551

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 270

Met Pro Thr Pro Gly Ala Ala Ser Leu Leu Ser Ala Val Gln Ala Gln  
 1 5 10 15  
 Glu Arg Arg Leu Tyr Val Pro Leu Pro Gly Gly Phe Ser Val Pro Pro  
 20 25 30  
 Val Thr Pro Met Pro His Cys Leu Leu Asp Pro Lys Glu Asp Leu Lys  
 35 40 45  
 Gly Cys Pro Gln Ala Cys Ser Gly Cys Ser Met Gly Thr Pro Ala Pro  
 50 55 60  
 Ser Tyr Leu Val Gln Gly Ala Gln Gly Met Pro Leu Arg Lys Ala Ala  
 65 70 75 80  
 Ser Leu Ala Thr Lys Leu Glu Glu Met Gly Leu Phe Gly Gln Gln Cys  
 85 90 95  
 Leu Pro Ala Met Gly Tyr Thr Cys Arg Cys Arg Glu Pro Leu Leu  
 100 105 110  
 Pro Ser His Leu Ile Gly Val Gly Phe Pro Gln Ala Pro Ala Pro Gln  
 115 120 125  
 Leu Leu Ser Ala Leu Leu Leu Leu Pro Ala Pro Pro Ser Pro Ala Gln  
 130 135 140  
 Ser Glu Val His Pro Pro Val Arg Gly Ala Glu Gln Cys Cys Lys Leu  
 145 150 155 160  
 Ser Ala Pro Glu Tyr Pro Gly Asp Leu Leu Asn Cys Thr Phe Ser Phe  
 165 170 175  
 Cys Lys Pro Glu Leu Ser Leu Cys Thr Ser Asn Leu Leu Pro Gly Asn  
 180 185 190  
 Ala Ala Val Thr Glu Gln Ser Gly Lys Val Leu Asp Asn Thr Leu Gly  
 195 200 205  
 Gly Asn Phe Ser Leu Lys Cys Ile Gly Ala Glu Thr Arg Thr Pro Cys  
 210 215 220  
 Gln Ala Ala Leu Trp Val Phe Glu Ala Lys Val Ser Arg Leu Met Lys  
 225 230 235 240  
 Ser Ala Ser Cys Gln Arg Gln Arg Ile His Trp Gln Gln Gly Ala Leu  
 245 250 255  
 Ala Ala Val Arg Gln Gly Asp Leu Gly Leu Lys Tyr Lys Glu Ile Ser  
 260 265 270  
 Cys Lys Asp Ala Gly Val Phe His Gly Thr Ser Ser Ser Gly Lys Leu  
 275 280 285  
 His Ser His Gly Lys Thr Leu Glu Pro Glu Ser Gly Lys Ala Ile Arg  
 290 295 300  
 Ala Trp Ile Leu Glu Ile Leu Ser Ser Cys Lys Pro Gly Ser Leu Val  
 305 310 315 320  
 Gln Met Ala Lys Asn Met Thr Met Asp Arg Ala Cys Ala Tyr Leu Val  
 325 330 335

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Thr Cys Arg Glu Ala Thr Leu Trp Trp Gly Val Val Ala Gly Ser Leu  
 Val Tyr Glu 340 His Gly Asn Gln Lys 345 Pro Ile Pro Val Thr Val Trp Arg  
 Gly Gly Glu Arg Arg Gly Met Val Pro Thr Lys Lys Asp Thr Ser Thr  
 Ser Val Leu Phe Ile Gln Ile His Val Leu Thr Phe Ser Ala Glu Asn  
 385 390 395 400  
 Lys Ile Gln Ser Asn Cys Asn Ser Ser Ser Cys Ile Arg Pro Thr Gly  
 405 410 415  
 Arg Arg Glu Arg Asp Val Thr Asn Gln Thr His Ala Ser Gly Lys Arg  
 420 425 430  
 Cys Val Ala Gly Leu Ala Pro Glu Gly Ser Asp Glu Gly Leu Leu Pro  
 435 440 445  
 Ala Thr Leu Pro Cys Leu Gly Phe Pro Lys Leu Leu Ser Ala Glu Glu  
 450 455 460  
 Arg Ala Asn His Gly Gln Pro Arg Asn Thr Arg Pro Cys Gln Leu Asp  
 465 470 475 480  
 Leu Asp Cys Ala Ile Phe Gly His Phe His Thr Leu Pro Asn Lys Leu  
 485 490 495  
 Leu Leu Val Ser Val Ser Glu Ile Leu Thr Ser Glu Ile Leu Thr Leu  
 500 505 510  
 Ala Asn Leu Leu Gln Gly Cys Gln His Glu Pro Glu Arg Tyr Gly His  
 515 520 525  
 Val Thr Asp Pro Glu His Lys Thr Thr Ser Ala Phe Thr Val Ser Lys  
 530 535 540  
 Ala Ser Arg Trp Arg Lys Asn  
 545 550

&lt;210&gt; 271

&lt;211&gt; 2779

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 271

Met Gln Gly Asp Leu Lys Thr Thr Asp Ile Ser Ile Glu Pro Pro Ser  
 1 5 10 15  
 Ala Gln Leu Glu Val Gln Ala Gly Gln Val Asp Leu Lys Leu Pro Glu  
 20 25 30  
 Gly His Val Pro Glu Gly Ala Gly Leu Lys Gly His Leu Pro Lys Leu  
 35 40 45  
 Gln Met Pro Ser Phe Lys Met Pro Lys Val Asp Arg Lys Gly Pro Gln  
 50 55 60  
 Ile Asp Val Lys Gly Pro Lys Leu Asp Leu Lys Gly Pro Lys Thr Asp  
 65 70 75 80  
 Val Thr Ala Pro Asp Val Glu Val Ser Gln Pro Gly Met Glu Val Asp  
 85 90 95  
 Val Glu Ala Pro Gly Ala Lys Leu Asp Gly Ala Arg Leu Glu Gly Asp  
 100 105 110  
 Leu Ser Leu Ala Asp Lys Asp Val Thr Ala Lys Asp Ser Lys Phe Lys  
 115 120 125  
 Met Pro Lys Phe Lys Met Pro Ser Phe Gly Val Ser Ala Pro Gly Lys  
 130 135 140  
 Ser Ile Glu Val Leu Val Asp Val Ser Ala Pro Lys Val Glu Ala Asp  
 145 150 155 160  
 Leu Ser Leu Pro Ser Met Gln Gly Asp Leu Lys Asn Thr Asp Ile Ser  
 165 170 175

Ile	Glu	Pro	Pro	Ser	Ala	Gln	Leu	Glu	Val	Gln	Ala	Gly	Gln	Val	Asp
Val	Lys	Leu	180	Glu	Gly	His	Val	185	Glu	Gly	Ala	Gly	190	Lys	Gly
His	Leu	Pro	195	Leu	Gln	Met	200	Pro	Ser	Phe	Lys	Met	205	Pro	Asp
Arg	Lys	Gly	210	Pro	Gln	Ile	215	Ile	Lys	Gly	Pro	Lys	220	Leu	Lys
Gly	Pro	Lys	225	Met	Asp	Val	230	Ala	Pro	Asp	Val	Glu	235	Ser	Gln
Ser	Met	Glu	245	Val	Asp	Val	250	Ala	Pro	Gly	Ala	Lys	255	Leu	Asp
Arg	Leu	Glu	260	Gly	Asp	Leu	265	Ala	Asp	Lys	Asp	Val	270	Thr	Ala
Asp	Ser	Lys	275	Phe	Lys	Met	280	Phe	Lys	Met	Pro	Ser	285	Tyr	Arg
Ser	Ala	Pro	290	Gly	Lys	Ser	295	Ile	Gln	Ala	Ser	Val	300	Ser	Ala
Lys	Ala	Glu	305	Ala	Asp	Val	310	Ser	Leu	Pro	Ser	Met	315	Gln	Gly
Thr	Thr	Asp	325	Leu	Ser	Ile	330	Leu	Pro	Ser	Val	Asp	335	Leu	Glu
Ala	Gly	Gln	340	Val	Asp	Val	345	Leu	Pro	Glu	Gly	His	350	Val	Pro
Ala	Gly	Leu	355	Lys	Gly	His	360	Leu	Pro	Lys	Val	Glu	365	Met	Pro
Met	Pro	Lys	370	Val	Asp	Leu	375	Lys	Ser	Pro	Gln	Val	380	Asp	Ile
Lys	Leu	Asp	385	Leu	Lys	Val	390	Pro	Lys	Ala	Glu	Val	395	Thr	Val
Glu	Val	Ser	405	Pro	Ser	Val	410	Glu	Val	Asp	Val	Gln	415	Ala	Pro
Lys	Leu	Asp	420	Gly	Ala	Arg	425	Glu	Gly	Asp	Leu	Ser	430	Leu	Ala
Asp	Val	Thr	435	Ala	Lys	Asp	440	Ser	Lys	Phe	Lys	Met	445	Pro	Lys
Pro	Ser	Phe	450	Gly	Val	Ser	455	Ala	Pro	Gly	Arg	Ser	460	Ile	Glu
Asp	Val	Ser	465	Ala	Pro	Lys	470	Val	Glu	Ala	Asp	Val	475	Ser	Leu
Gln	Gly	Asp	485	Leu	Lys	Ala	490	Thr	Asp	Leu	Ser	Ile	495	Gln	Pro
Asp	Leu	Glu	500	Val	Gln	Ala	505	Gln	Val	Asp	Val	Glu	510	Leu	Leu
Pro	Val	Pro	515	Glu	Gly	Ala	520	Leu	Lys	Gly	His	Leu	525	Pro	Lys
Met	Pro	Ser	530	Leu	Lys	Thr	535	Pro	Lys	Val	Asp	Leu	540	Lys	Gly
Asp	Val	Lys	545	Gly	Pro	Lys	550	Leu	Asp	Leu	Lys	Gly	555	Pro	Lys
Arg	Val	Pro	565	Asp	Val	Glu	570	Ser	Leu	Pro	Ser	Val	575	Glu	Val
Gln	Ala	Pro	580	Lys	Ala	Lys	585	Leu	Asp	Ala	Gly	Arg	590	Leu	Glu
Ser	Leu	Ala	595	Asp	Lys	Asp	600	Thr	Ala	Lys	Asp	Ser	605	Lys	Phe
Pro	Lys	Phe	610	Lys	Met	Pro	615	Ser	Phe	Arg	Val	Ser	620	Ala	Pro
Met	Glu	Ala	625	Ser	Val	Asp	630	Ser	Ala	Pro	Lys	Val	635	Glu	Ala
Ser	Leu	Pro	645	Ser	Met	Gln	650	Gly	Asp	Leu	Lys	Thr	655	Thr	Asp
			660				665						670	Leu	Ser

Gln Pro Pro Ser Ala Asp Leu Lys Val Gln Ala Gly Gln Met Asp Val  
 675 680 685  
 Lys Leu Pro Glu Gly Gln Val Pro Glu Gly Ala Gly Leu Lys Glu His  
 690 695 700  
 Leu Pro Lys Val Glu Met Pro Ser Leu Lys Met Pro Lys Val Asp Leu  
 705 710 715 720  
 Lys Gly Pro Gln Val Asp Ile Lys Gly Pro Lys Leu Asp Leu Lys Val  
 725 730 735  
 Ser Lys Ala Glu Val Thr Ala Pro Asp Val Glu Val Ser Leu Pro Ser  
 740 745 750  
 Val Glu Val Asp Val Gln Ala Pro Arg Ala Lys Leu Asp Ser Ala Gln  
 755 760 765  
 Leu Glu Gly Asp Leu Ser Leu Ala Asp Lys Asp Val Thr Ala Lys Asp  
 770 775 780  
 Ser Lys Phe Lys Met Pro Lys Phe Lys Met Pro Ser Phe Gly Val Ser  
 785 790 795 800  
 Ala Pro Gly Lys Ser Ile Glu Ala Ser Val His Val Ser Ala Pro Lys  
 805 810 815  
 Val Glu Ala Asp Val Ser Leu Pro Ser Met Gln Gly Asp Leu Lys Thr  
 820 825 830  
 Thr Asp Leu Ser Ile Gln Pro His Ser Ala Asp Leu Thr Val Gln Ala  
 835 840 845  
 Arg Gln Val Asp Met Lys Leu Leu Glu Gly His Val Pro Glu Glu Ala  
 850 855 860  
 Gly Leu Lys Gly His Leu Pro Lys Val Gln Met Pro Ser Phe Lys Met  
 865 870 875 880  
 Pro Lys Val Asp Leu Lys Gly Pro Glu Ile Asp Ile Lys Gly Pro Lys  
 885 890 895  
 Leu Asp Leu Lys Asp Pro Lys Val Glu Val Thr Ala Pro Asp Val Glu  
 900 905 910  
 Val Ser Leu Pro Ser Val Glu Val Asp Val Glu Ala Pro Gly Ala Lys  
 915 920 925  
 Leu Asp Gly Ala Arg Leu Glu Gly Asp Leu Ser Leu Ala Asp Lys Asp  
 930 935 940  
 Met Thr Ala Lys Asp Ser Lys Phe Lys Met Pro Lys Phe Lys Met Pro  
 945 950 955 960  
 Ser Phe Gly Val Ser Ala Pro Gly Lys Ser Met Glu Ala Ser Val Asp  
 965 970 975  
 Val Thr Ala Pro Lys Val Glu Ala Asp Val Ser Leu Pro Ser Met Gln  
 980 985 990  
 Gly Asp Leu Lys Ala Thr Asp Leu Ser Val Gln Pro Pro Ser Ala Asp  
 995 1000 1005  
 Leu Glu Val Gln Ala Gly Gln Val Asp Val Lys Leu Pro Glu Gly  
 1010 1015 1020  
 Pro Val Pro Glu Gly Ala Ser Leu Lys Gly His Leu Pro Lys Val  
 1025 1030 1035  
 Gln Met Pro Ser Phe Lys Met Pro Lys Val Asp Leu Lys Gly Pro  
 1040 1045 1050  
 Gln Ile Asp Val Lys Gly Pro Lys Leu Asp Leu Lys Gly Pro Lys  
 1055 1060 1065  
 Ala Glu Val Thr Ala Pro Asp Val Lys Met Ser Leu Ser Ser Met  
 1070 1075 1080  
 Glu Val Asp Val Gln Ala Pro Arg Ala Lys Leu Asp Gly Val Gln  
 1085 1090 1095  
 Leu Glu Gly Asp Leu Ser Leu Ala Asp Lys Asp Val Thr Ala Lys  
 1100 1105 1110  
 Asp Ser Lys Phe Lys Met Pro Lys Phe Lys Met Pro Ser Phe Gly  
 1115 1120 1125  
 Val Ser Ala Pro Gly Lys Ser Met Glu Ala Ser Val Asp Val Ser  
 1130 1135 1140  
 Glu Leu Lys Ala Lys Ala Asp Val Ser Leu Pro Ser Met Gln Gly  
 1145 1150 1155

Asp	Leu	Lys	Thr	Thr	Asp	Leu	Ser	Ile	Gln	Ser	Pro	Ser	Ala	Asp
1160						1165					1170			
Leu	Glu	Val	Gln	Ala	Gly	Gln	Val	Asp	Val	Lys	Leu	Pro	Glu	Gly
1175						1180					1185			
Pro	Leu	Pro	Lys	Gly	Ala	Gly	Leu	Lys	Gly	His	Leu	Pro	Lys	Val
1190						1195					1200			
Gln	Met	Pro	Cys	Leu	Lys	Met	Pro	Lys	Val	Ala	Leu	Lys	Gly	Pro
1205						1210					1215			
Gln	Val	Asp	Val	Lys	Gly	Pro	Lys	Leu	Asp	Leu	Lys	Gly	Pro	Lys
1220						1225					1230			
Ala	Asp	Val	Met	Thr	Pro	Val	Val	Glu	Val	Ser	Leu	Pro	Ser	Met
1235						1240					1245			
Glu	Val	Asp	Val	Glu	Ala	Pro	Gly	Ala	Lys	Leu	Asp	Ser	Val	Arg
1250						1255					1260			
Leu	Glu	Gly	Asp	Leu	Ser	Leu	Ala	Asp	Lys	Asp	Met	Thr	Ala	Lys
1265						1270					1275			
Asp	Ser	Lys	Phe	Lys	Met	Pro	Lys	Phe	Lys	Met	Pro	Ser	Phe	Gly
1280						1285					1290			
Val	Ser	Ala	Pro	Gly	Lys	Ser	Ile	Glu	Ala	Ser	Leu	Asp	Val	Ser
1295						1300					1305			
Ala	Leu	Lys	Val	Glu	Ala	Asp	Val	Ser	Leu	Pro	Ser	Met	Gln	Gly
1310						1315					1320			
Asp	Leu	Lys	Thr	Thr	His	Leu	Ser	Ile	Gln	Pro	Pro	Ser	Ala	Asp
1325						1330					1335			
Leu	Glu	Val	Gln	Ala	Gly	Gln	Glu	Asp	Val	Lys	Leu	Pro	Glu	Gly
1340						1345					1350			
Pro	Val	His	Glu	Gly	Ala	Gly	Leu	Lys	Gly	His	Leu	Pro	Lys	Leu
1355						1360					1365			
Gln	Met	Pro	Ser	Phe	Lys	Val	Pro	Lys	Val	Asp	Leu	Lys	Gly	Pro
1370						1375					1380			
Gln	Ile	Asp	Val	Asn	Val	Pro	Lys	Leu	Asp	Leu	Lys	Gly	Pro	Lys
1385						1390					1395			
Val	Glu	Val	Thr	Ser	Pro	Asn	Leu	Asp	Val	Ser	Leu	Pro	Ser	Met
1400						1405					1410			
Glu	Val	Asp	Ile	Gln	Ala	Pro	Gly	Ala	Lys	Leu	Asp	Ser	Thr	Arg
1415						1420					1425			
Leu	Glu	Gly	Asp	Leu	Ser	Leu	Ala	Asp	Lys	Asp	Val	Thr	Ala	Lys
1430						1435					1440			
Asp	Ser	Lys	Phe	Lys	Met	Pro	Lys	Phe	Lys	Met	Pro	Ser	Phe	Gly
1445						1450					1455			
Met	Leu	Ser	Pro	Gly	Lys	Ser	Ile	Glu	Val	Ser	Val	Asp	Val	Ser
1460						1465					1470			
Ala	Pro	Lys	Met	Glu	Ala	Asp	Met	Ser	Ile	Pro	Ser	Met	Gln	Gly
1475						1480					1485			
Asp	Leu	Lys	Thr	Thr	Asp	Leu	Arg	Ile	Gln	Ala	Pro	Ser	Ala	Asp
1490						1495					1500			
Leu	Glu	Val	Gln	Ala	Gly	Gln	Val	Asp	Leu	Lys	Leu	Pro	Glu	Gly
1505						1510					1515			
His	Met	Pro	Glu	Val	Ala	Gly	Leu	Lys	Gly	His	Leu	Pro	Lys	Val
1520						1525					1530			
Glu	Met	Pro	Ser	Phe	Lys	Met	Pro	Lys	Val	Asp	Leu	Lys	Gly	Pro
1535						1540					1545			
Gln	Val	Asp	Val	Lys	Gly	Pro	Lys	Leu	Asp	Leu	Lys	Gly	Pro	Lys
1550						1555					1560			
Ala	Glu	Val	Met	Ala	Pro	Asp	Val	Glu	Val	Ser	Leu	Pro	Ser	Val
1565						1570					1575			
Glu	Thr	Asp	Val	Gln	Ala	Pro	Gly	Ser	Met	Leu	Asp	Gly	Ala	Arg
1580						1585					1590			
Leu	Glu	Gly	Asp	Leu	Ser	Leu	Ala	His	Glu	Asp	Val	Ala	Gly	Lys
1595						1600					1605			
Asp	Ser	Lys	Phe	Gln	Gly	Pro	Lys	Leu	Ser	Thr	Ser	Gly	Phe	Glu
1610						1615					1620			

Trp	Ser	Ser	Lys	Lys	Val	Ser	Met	Ser	Ser	Ser	Glu	Ile	Glu	Gly
1625						1630					1635			
Asn	Val	Thr	Phe	His	Glu	Lys	Thr	Ser	Thr	Phe	Pro	Ile	Val	Glu
1640						1645					1650			
Ser	Val	Val	His	Glu	Gly	Asp	Leu	His	Asp	Pro	Ser	Arg	Asp	Gly
1655						1660					1665			
Asn	Leu	Gly	Leu	Ala	Val	Gly	Glu	Val	Gly	Met	Asp	Ser	Lys	Phe
1670						1675					1680			
Lys	Lys	Leu	His	Phe	Lys	Val	Pro	Lys	Val	Ser	Phe	Ser	Ser	Thr
1685						1690					1695			
Lys	Thr	Pro	Lys	Asp	Ser	Leu	Val	Pro	Gly	Ala	Lys	Ser	Ser	Ile
1700						1705					1710			
Gly	Leu	Ser	Thr	Ile	Pro	Leu	Ser	Ser	Ser	Glu	Cys	Ser	Ser	Phe
1715						1720					1725			
Glu	Leu	Gln	Gln	Val	Ser	Ala	Cys	Ser	Glu	Pro	Ser	Met	Gln	Met
1730						1735					1740			
Pro	Lys	Val	Gly	Phe	Ala	Gly	Phe	Pro	Ser	Ser	Arg	Leu	Asp	Leu
1745						1750					1755			
Thr	Gly	Pro	His	Phe	Glu	Ser	Ser	Ile	Leu	Ser	Pro	Cys	Glu	Asp
1760						1765					1770			
Val	Thr	Leu	Thr	Lys	Tyr	Gln	Val	Thr	Val	Pro	Arg	Ala	Ala	Leu
1775						1780					1785			
Ala	Pro	Glu	Leu	Ala	Leu	Glu	Ile	Pro	Ser	Gly	Ser	Gln	Ala	Asp
1790						1795					1800			
Ile	Pro	Leu	Pro	Lys	Thr	Glu	Cys	Ser	Thr	Asp	Leu	Gln	Pro	Pro
1805						1810					1815			
Glu	Gly	Val	Pro	Thr	Ser	Gln	Ala	Glu	Ser	His	Ser	Gly	Pro	Leu
1820						1825					1830			
Asn	Ser	Met	Ile	Pro	Val	Ser	Leu	Gly	Gln	Val	Ser	Phe	Pro	Lys
1835						1840					1845			
Phe	Tyr	Lys	Pro	Lys	Phe	Val	Phe	Ser	Val	Pro	Gln	Met	Ala	Val
1850						1855					1860			
Pro	Glu	Gly	Asp	Leu	His	Ala	Ala	Val	Gly	Ala	Pro	Val	Met	Ser
1865						1870					1875			
Pro	Leu	Ser	Pro	Gly	Glu	Arg	Val	Gln	Cys	Pro	Leu	Pro	Ser	Thr
1880						1885					1890			
Gln	Leu	Pro	Ser	Pro	Gly	Thr	Cys	Val	Ser	Gln	Gly	Pro	Glu	Glu
1895						1900					1905			
Leu	Val	Ala	Ser	Leu	Gln	Thr	Ser	Val	Val	Ala	Pro	Gly	Glu	Ala
1910						1915					1920			
Pro	Ser	Glu	Asp	Ala	Asp	His	Glu	Gly	Lys	Gly	Ser	Pro	Leu	Lys
1925						1930					1935			
Met	Pro	Lys	Ile	Lys	Leu	Pro	Ser	Phe	Arg	Trp	Ser	Pro	Lys	Lys
1940						1945					1950			
Glu	Thr	Gly	Pro	Lys	Val	Asp	Pro	Glu	Cys	Ser	Val	Glu	Asp	Ser
1955						1960					1965			
Lys	Leu	Ser	Leu	Val	Leu	Asp	Lys	Asp	Glu	Val	Ala	Pro	Gln	Ser
1970						1975					1980			
Ala	Ile	His	Met	Asp	Leu	Pro	Pro	Glu	Arg	Asp	Gly	Glu	Lys	Gly
1985						1990					1995			
Arg	Ser	Thr	Lys	Pro	Gly	Phe	Ala	Met	Pro	Lys	Leu	Ala	Leu	Pro
2000						2005					2010			
Lys	Met	Lys	Ala	Ser	Lys	Ser	Gly	Val	Ser	Leu	Pro	Gln	Arg	Asp
2015						2020					2025			
Val	Asp	Pro	Ser	Leu	Ser	Ser	Ala	Thr	Ala	Gly	Gly	Ser	Phe	Gln
2030						2035					2040			
Asp	Thr	Glu	Lys	Ala	Ser	Ser	Asp	Gly	Gly	Arg	Gly	Gly	Leu	Gly
2045						2050					2055			
Ala	Thr	Ala	Ser	Ala	Thr	Gly	Ser	Glu	Gly	Val	Asn	Leu	His	Arg
2060						2065					2070			
Pro	Gln	Val	His	Ile	Pro	Ser	Leu	Gly	Phe	Ala	Lys	Pro	Asp	Leu
2075						2080					2085			

Arg	Ser	Ser	Lys	Ala	Lys	Val	Glu	Val	Ser	Gln	Pro	Glu	Ala	Asp
2090						2095					2100			
Leu	Pro	Leu	Pro	Lys	His	Asp	Leu	Ser	Thr	Glu	Gly	Asp	Ser	Arg
2105						2110					2115			
Gly	Cys	Gly	Leu	Gly	Asp	Val	Pro	Val	Ser	Gln	Pro	Cys	Gly	Glu
2120						2125					2130			
Gly	Ile	Ala	Pro	Thr	Pro	Glu	Asp	Pro	Leu	Gln	Pro	Ser	Cys	Arg
2135						2140					2145			
Lys	Pro	Asp	Ala	Glu	Val	Leu	Thr	Val	Glu	Ser	Pro	Glu	Glu	Glu
2150						2155					2160			
Ala	Met	Thr	Lys	Tyr	Ser	Gln	Glu	Ser	Trp	Phe	Lys	Met	Pro	Lys
2165						2170					2175			
Phe	Arg	Met	Pro	Ser	Leu	Arg	Arg	Ser	Phe	Arg	Asp	Arg	Gly	Gly
2180						2185					2190			
Ala	Gly	Lys	Leu	Glu	Val	Ala	Gln	Thr	Gln	Ala	Pro	Ala	Ala	Thr
2195						2200					2205			
Gly	Gly	Glu	Ala	Ala	Ala	Lys	Val	Lys	Glu	Phe	Leu	Val	Ser	Gly
2210						2215					2220			
Ser	Asn	Val	Glu	Ala	Ala	Met	Ser	Leu	Gln	Leu	Pro	Glu	Ala	Asp
2225						2230					2235			
Ala	Glu	Val	Thr	Ala	Ser	Glu	Ser	Lys	Ser	Ser	Thr	Asp	Ile	Leu
2240						2245					2250			
Arg	Cys	Asp	Leu	Asp	Ser	Thr	Gly	Leu	Lys	Leu	His	Leu	Ser	Thr
2255						2260					2265			
Ala	Gly	Met	Thr	Gly	Asp	Glu	Leu	Ser	Thr	Ser	Glu	Val	Arg	Ile
2270						2275					2280			
His	Pro	Ser	Lys	Gly	Pro	Leu	Pro	Phe	Gln	Met	Pro	Gly	Met	Arg
2285						2290					2295			
Leu	Pro	Glu	Thr	Gln	Val	Leu	Pro	Gly	Glu	Ile	Asp	Glu	Thr	Pro
2300						2305					2310			
Leu	Ser	Lys	Pro	Gly	His	Asp	Leu	Ala	Ser	Met	Glu	Asp	Lys	Thr
2315						2320					2325			
Glu	Lys	Trp	Ser	Ser	Gln	Pro	Glu	Gly	Pro	Leu	Lys	Leu	Lys	Ala
2330						2335					2340			
Ser	Ser	Thr	Asp	Met	Pro	Ser	Gln	Ile	Ser	Val	Val	Asn	Val	Asp
2345						2350					2355			
Gln	Leu	Trp	Glu	Asp	Ser	Val	Leu	Thr	Val	Lys	Phe	Pro	Lys	Leu
2360						2365					2370			
Met	Val	Pro	Arg	Phe	Ser	Phe	Pro	Ala	Pro	Ser	Ser	Glu	Asp	Asp
2375						2380					2385			
Val	Phe	Ile	Pro	Thr	Val	Arg	Glu	Val	Gln	Cys	Pro	Glu	Ala	Asn
2390						2395					2400			
Ile	Asp	Thr	Ala	Leu	Cys	Lys	Glu	Ser	Pro	Gly	Leu	Trp	Gly	Ala
2405						2410					2415			
Ser	Ile	Leu	Lys	Ala	Gly	Ala	Gly	Val	Pro	Gly	Glu	Gln	Pro	Val
2420						2425					2430			
Asp	Leu	Asn	Leu	Pro	Leu	Glu	Ala	Pro	Pro	Ile	Ser	Lys	Val	Arg
2435						2440					2445			
Val	His	Ile	Gln	Gly	Ala	Gln	Val	Glu	Ser	Gln	Glu	Val	Thr	Ile
2450						2455					2460			
His	Ser	Ile	Val	Thr	Pro	Glu	Phe	Val	Asp	Leu	Ser	Val	Pro	Arg
2465						2470					2475			
Thr	Phe	Ser	Thr	Gln	Ile	Val	Arg	Glu	Ser	Glu	Ile	Pro	Thr	Ser
2480						2485					2490			
Glu	Ile	Gln	Thr	Pro	Ser	Tyr	Gly	Phe	Ser	Leu	Leu	Lys	Val	Lys
2495						2500					2505			
Ile	Pro	Glu	Pro	His	Thr	Gln	Ala	Arg	Val	Tyr	Thr	Thr	Met	Thr
2510						2515					2520			
Gln	His	Ser	Arg	Thr	Gln	Glu	Gly	Thr	Glu	Glu	Ala	Pro	Ile	Gln
2525						2530					2535			
Ala	Thr	Pro	Gly	Val	Asp	Ser	Ile	Ser	Gly	Asp	Leu	Gln	Pro	Asp
2540						2545					2550			



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Thr	Gly	Glu	Pro	Phe	Glu	Met	Ile	Ser	Ser	Ser	Val	Asn	Val	Leu
2555						2560					2565			
Gly	Gln	Gln	Thr	Leu	Thr	Phe	Glu	Val	Pro	Ser	Gly	His	Gln	Leu
2570						2575					2580			
Ala	Asp	Ser	Cys	Ser	Asp	Glu	Glu	Pro	Ala	Glu	Ile	Leu	Glu	Phe
2585						2590					2595			
Pro	Pro	Asp	Asp	Ser	Gln	Glu	Ala	Thr	Thr	Pro	Leu	Ala	Asp	Glu
2600						2605					2610			
Gly	Arg	Ala	Pro	Lys	Asp	Lys	Pro	Glu	Ser	Lys	Lys	Ser	Gly	Leu
2615						2620					2625			
Leu	Trp	Phe	Trp	Leu	Pro	Asn	Ile	Gly	Phe	Ser	Ser	Ser	Val	Asp
2630						2635					2640			
Glu	Thr	Gly	Val	Asp	Ser	Lys	Asn	Asp	Val	Gln	Arg	Ser	Ala	Pro
2645						2650					2655			
Ile	Gln	Thr	Gln	Pro	Glu	Ala	Arg	Pro	Glu	Ala	Glu	Leu	Pro	Lys
2660						2665					2670			
Lys	Gln	Glu	Lys	Ala	Gly	Trp	Phe	Arg	Phe	Pro	Lys	Leu	Gly	Phe
2675						2680					2685			
Ser	Ser	Ser	Pro	Thr	Lys	Lys	Ser	Lys	Ser	Thr	Glu	Asp	Gly	Ala
2690						2695					2700			
Glu	Leu	Glu	Glu	Gln	Lys	Leu	Gln	Glu	Glu	Thr	Ile	Thr	Phe	Phe
2705						2710					2715			
Asp	Ala	Arg	Glu	Ser	Phe	Ser	Pro	Glu	Glu	Lys	Glu	Glu	Gly	Glu
2720						2725					2730			
Leu	Ile	Gly	Pro	Val	Gly	Thr	Gly	Leu	Asp	Ser	Arg	Val	Met	Val
2735						2740					2745			
Thr	Ser	Ala	Ala	Arg	Thr	Glu	Leu	Ile	Leu	Pro	Glu	Gln	Asp	Arg
2750						2755					2760			
Lys	Ala	Asp	Asp	Glu	Ser	Lys	Gly	Ser	Gly	Leu	Gly	Pro	Asn	Glu
2765						2770					2775			
Gly														

&lt;210&gt; 272

&lt;211&gt; 512

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 272

Met	Asp	Phe	Glu	Ser	Gly	Gln	Val	Asp	Pro	Leu	Ala	Ser	Val	Ile	Leu
1				5					10					15	
Pro	Pro	Asn	Leu	Leu	Glu	Asn	Leu	Ser	Pro	Glu	Asp	Ser	Val	Leu	Val
		20						25					30		
Arg	Arg	Ala	Gln	Phe	Thr	Phe	Phe	Asn	Lys	Thr	Gly	Leu	Phe	Gln	Asp
		35				40						45			
Val	Gly	Pro	Gln	Arg	Lys	Thr	Leu	Val	Ser	Tyr	Val	Met	Ala	Cys	Ser
	50					55					60				
Ile	Gly	Asn	Ile	Thr	Ile	Gln	Asn	Leu	Lys	Asp	Pro	Val	Gln	Ile	Lys
65					70					75				80	
Ile	Lys	His	Thr	Arg	Thr	Gln	Glu	Val	His	His	Pro	Ile	Cys	Ala	Phe
			85						90					95	
Trp	Asp	Leu	Asn	Lys	Asn	Lys	Ser	Phe	Gly	Gly	Trp	Asn	Thr	Ser	Gly
		100						105					110		
Cys	Val	Ala	His	Arg	Asp	Ser	Asp	Ala	Ser	Glu	Thr	Val	Cys	Leu	Cys
		115					120					125			
Asn	His	Phe	Thr	His	Phe	Gly	Val	Leu	Met	Asp	Leu	Pro	Arg	Ser	Ala
130						135						140			

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Ser Gln Leu Asp Ala Arg Asn Thr Lys Val Leu Thr Phe Ile Ser Tyr  
 145 150 155 160  
 Ile Gly Cys Gly Ile Ser Ala Ile Phe Ser Ala Ala Thr Leu Leu Thr  
 165 170 175  
 Tyr Val Ala Phe Glu Lys Leu Arg Arg Asp Tyr Pro Ser Lys Ile Leu  
 180 185 190  
 Met Asn Leu Ser Thr Ala Leu Leu Phe Leu Asn Leu Leu Phe Leu Leu  
 195 200 205  
 Asp Gly Trp Ile Thr Ser Phe Asn Val Asp Gly Leu Cys Ile Ala Val  
 210 215 220  
 Ala Val Leu Leu His Phe Phe Leu Leu Ala Thr Phe Thr Trp Met Gly  
 225 230 235 240  
 Leu Glu Ala Ile His Met Tyr Ile Ala Leu Val Lys Val Phe Asn Thr  
 245 250 255  
 Tyr Ile Arg Arg Tyr Ile Leu Lys Phe Cys Ile Ile Gly Trp Gly Leu  
 260 265 270  
 Pro Ala Leu Val Val Ser Val Val Leu Ala Ser Arg Asn Asn Asn Glu  
 275 280 285  
 Val Tyr Gly Lys Glu Ser Tyr Gly Lys Glu Lys Gly Asp Glu Phe Cys  
 290 295 300  
 Trp Ile Gln Asp Pro Val Ile Phe Tyr Val Thr Cys Ala Gly Tyr Phe  
 305 310 315 320  
 Gly Val Met Phe Phe Leu Asn Ile Ala Met Phe Ile Val Val Met Val  
 325 330 335  
 Gln Ile Cys Gly Arg Asn Gly Lys Arg Ser Asn Arg Thr Leu Arg Glu  
 340 345 350  
 Glu Val Leu Arg Asn Leu Arg Ser Val Val Ser Leu Thr Phe Leu Leu  
 355 360 365  
 Gly Met Thr Trp Gly Phe Ala Phe Phe Ala Trp Gly Pro Leu Asn Ile  
 370 375 380  
 Pro Phe Met Tyr Leu Phe Ser Ile Phe Asn Ser Leu Gln Gly Leu Phe  
 385 390 395 400  
 Ile Phe Ile Phe His Cys Ala Met Lys Glu Asn Val Gln Lys Gln Trp  
 405 410 415  
 Arg Arg His Leu Cys Cys Gly Arg Phe Arg Leu Ala Asp Asn Ser Asp  
 420 425 430  
 Trp Ser Lys Thr Ala Thr Asn Ile Ile Lys Lys Ser Ser Asp Asn Leu  
 435 440 445  
 Gly Lys Ser Leu Ser Ser Ser Ser Ile Gly Ser Asn Ser Thr Tyr Leu  
 450 455 460  
 Thr Ser Lys Ser Lys Ser Ser Ser Thr Thr Tyr Phe Lys Arg Asn Ser  
 465 470 475 480  
 His Thr Asp Asn Val Ser Tyr Glu His Ser Phe Asn Lys Ser Gly Ser  
 485 490 495  
 Leu Arg Gln Cys Phe His Gly Gln Val Leu Val Lys Thr Gly Pro Cys  
 500 505 510

&lt;210&gt; 273

&lt;211&gt; 355

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 273

Met Ala Ala Pro Ala Phe Glu Pro Gly Arg Gln Ser Asp Leu Leu Val  
 1 5 10 15  
 Lys Leu Asn Arg Leu Met Glu Arg Cys Leu Arg Asn Ser Lys Cys Ile  
 20 25 30

Asp Thr Glu Ser Leu Cys Val Val Ala Gly Glu Lys Val Trp Gln Ile  
 35 40 45  
 Arg Val Asp Leu His Leu Leu Asn His Asp Gly Asn Ile Ile Asp Ala  
 50 55 60  
 Ala Ser Ile Ala Ala Ile Val Ala Leu Cys His Phe Arg Arg Pro Asp  
 65 70 75  
 Val Ser Val Gln Gly Asp Glu Val Thr Leu Tyr Thr Pro Glu Glu Arg  
 85 90 95  
 Asp Pro Val Pro Leu Ser Ile His His Met Pro Ile Cys Val Ser Phe  
 100 105 110  
 Ala Phe Phe Gln Gln Gly Thr Tyr Leu Leu Val Asp Pro Asn Glu Arg  
 115 120 125  
 Glu Glu Arg Val Met Asp Gly Leu Leu Val Ile Ala Met Asn Lys His  
 130 135 140  
 Arg Glu Ile Cys Thr Ile Gln Ser Ser Gly Gly Ile Met Leu Leu Lys  
 145 150 155 160  
 Asp Gln Val Leu Arg Cys Ser Lys Ile Ala Gly Val Lys Val Ala Glu  
 165 170 175  
 Ile Thr Glu Leu Ile Leu Lys Ala Leu Glu Asn Asp Gln Lys Val Arg  
 180 185 190  
 Lys Glu Gly Lys Phe Gly Phe Ala Glu Ser Ile Ala Asn Gln Arg  
 195 200 205  
 Ile Thr Ala Phe Lys Met Glu Lys Ala Pro Ile Asp Thr Ser Asp Val  
 210 215 220  
 Glu Glu Lys Ala Glu Glu Ile Ile Ala Glu Ala Glu Pro Pro Ser Glu  
 225 230 235 240  
 Val Val Ser Thr Pro Val Leu Trp Thr Pro Gly Thr Ala Gln Ile Gly  
 245 250 255  
 Glu Gly Val Glu Asn Ser Trp Gly Asp Leu Glu Asp Ser Glu Lys Glu  
 260 265 270  
 Asp Asp Glu Gly Gly Gly Asp Gln Ala Ile Ile Leu Asp Gly Ile Lys  
 275 280 285  
 Met Asp Thr Gly Val Glu Val Ser Asp Ile Gly Ser Gln Asp Ala Pro  
 290 295 300  
 Ile Ile Leu Ser Asp Ser Glu Glu Glu Glu Met Ile Ile Leu Glu Pro  
 305 310 315 320  
 Asp Lys Asn Pro Lys Lys Ile Arg Thr Gln Thr Thr Ser Ala Lys Gln  
 325 330 335  
 Glu Lys Ala Pro Ser Lys Lys Pro Val Lys Arg Arg Lys Lys Lys Arg  
 340 345 350  
 Ala Ala Asn  
 355

&lt;210&gt; 274

&lt;211&gt; 940

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 274

Met Ile Leu Glu Gln Tyr Val Val Val Ser Asn Tyr Lys Lys Gln Glu  
 1 5 10 15  
 Asn Ser Glu Leu Ser Leu Gln Ala Gly Glu Val Val Asp Val Ile Glu  
 20 25 30  
 Lys Asn Glu Ser Gly Trp Trp Phe Val Ser Thr Ser Glu Glu Gln Gly  
 35 40 45  
 Trp Val Pro Ala Thr Tyr Leu Glu Ala Gln Asn Gly Thr Arg Asp Asp  
 50 55 60

Ser	Asp	Ile	Asn	Thr	Ser	Lys	Thr	Gly	Glu	Glu	Glu	Lys	Tyr	Val	Thr
65					70					75					80
Val	Gln	Pro	Tyr	Thr	Ser	Gln	Ser	Lys	Asp	Glu	Ile	Gly	Phe	Glu	Lys
				85					90					95	
Gly	Val	Thr	Val	Glu	Val	Ile	Arg	Lys	Asn	Leu	Glu	Gly	Trp	Trp	Tyr
			100					105					110		
Ile	Arg	Tyr	Leu	Gly	Lys	Glu	Gly	Trp	Ala	Pro	Ala	Ser	Tyr	Leu	Lys
		115					120					125			
Lys	Ala	Lys	Asp	Asp	Leu	Pro	Thr	Arg	Lys	Lys	Asn	Leu	Ala	Gly	Pro
		130				135					140				
Val	Glu	Ile	Ile	Gly	Asn	Ile	Met	Glu	Ile	Ser	Asn	Leu	Leu	Asn	Lys
145					150					155					160
Lys	Ala	Ser	Gly	Asp	Lys	Glu	Thr	Pro	Pro	Ala	Glu	Gly	Glu	Gly	His
			165					170						175	
Glu	Ala	Pro	Ile	Ala	Lys	Lys	Glu	Ile	Ser	Leu	Pro	Ile	Leu	Cys	Asn
			180					185					190		
Ala	Ser	Asn	Gly	Ser	Ala	Val	Gly	Val	Pro	Asp	Arg	Thr	Val	Ser	Arg
		195					200					205			
Leu	Ala	Gln	Gly	Ser	Pro	Ala	Val	Ala	Arg	Ile	Ala	Pro	Gln	Arg	Ala
		210				215					220				
Gln	Ile	Ser	Ser	Pro	Asn	Leu	Arg	Thr	Arg	Pro	Pro	Pro	Arg	Arg	Glu
225					230					235					240
Ser	Ser	Leu	Gly	Phe	Gln	Leu	Pro	Lys	Pro	Pro	Glu	Pro	Pro	Ser	Val
			245					250						255	
Glu	Val	Glu	Tyr	Tyr	Thr	Ile	Ala	Glu	Phe	Gln	Ser	Cys	Ile	Ser	Asp
			260					265					270		
Gly	Ile	Ser	Phe	Arg	Gly	Gly	Gln	Lys	Ala	Glu	Val	Ile	Asp	Lys	Asn
		275				280						285			
Ser	Gly	Gly	Trp	Trp	Tyr	Val	Gln	Ile	Gly	Glu	Lys	Glu	Gly	Trp	Ala
		290				295					300				
Pro	Ala	Ser	Tyr	Ile	Asp	Lys	Arg	Lys	Lys	Pro	Asn	Leu	Ser	Arg	Arg
305					310					315					320
Thr	Ser	Thr	Leu	Thr	Arg	Pro	Lys	Val	Pro	Pro	Pro	Ala	Pro	Pro	Ser
			325						330					335	
Lys	Pro	Lys	Glu	Ala	Glu	Glu	Gly	Pro	Thr	Gly	Ala	Ser	Glu	Ser	Gln
			340					345					350		
Asp	Ser	Pro	Arg	Lys	Leu	Lys	Tyr	Glu	Glu	Pro	Glu	Tyr	Asp	Ile	Pro
		355					360					365			
Ala	Phe	Gly	Phe	Asp	Ser	Glu	Pro	Glu	Leu	Ser	Glu	Glu	Pro	Val	Glu
		370				375						380			
Asp	Arg	Ala	Ser	Gly	Glu	Arg	Arg	Pro	Ala	Gln	Pro	His	Arg	Pro	Ser
385					390					395					400
Pro	Ala	Ser	Ser	Leu	Gln	Arg	Ala	Arg	Phe	Lys	Val	Gly	Glu	Ser	Ser
			405						410					415	
Glu	Asp	Val	Ala	Leu	Glu	Glu	Glu	Thr	Ile	Tyr	Glu	Asn	Glu	Gly	Phe
			420					425					430		
Arg	Pro	Tyr	Ala	Glu	Asp	Thr	Leu	Ser	Ala	Arg	Gly	Ser	Ser	Gly	Asp
		435					440					445			
Ser	Asp	Ser	Pro	Gly	Ser	Ser	Ser	Leu	Ser	Leu	Thr	Arg	Lys	Asn	Ser
		450				455					460				
Pro	Lys	Ser	Gly	Ser	Pro	Lys	Ser	Ser	Ser	Leu	Leu	Lys	Leu	Lys	Ala
465					470					475					480
Glu	Lys	Asn	Ala	Gln	Ala	Glu	Met	Gly	Lys	Asn	His	Ser	Ser	Ala	Ser
			485						490					495	
Phe	Ser	Ser	Ser	Ile	Thr	Ile	Asn	Thr	Thr	Cys	Cys	Ser	Ser	Ser	Ser
			500						505					510	
Ser	Ser	Ser	Ser	Ser	Leu	Ser	Lys	Thr	Ser	Gly	Asp	Leu	Lys	Pro	Arg
		515					520					525			
Ser	Ala	Ser	Asp	Ala	Gly	Ile	Arg	Gly	Thr	Pro	Lys	Val	Arg	Ala	Lys
		530				535					540				
Lys	Asp	Ala	Asp	Ala	Asn	Ala	Gly	Leu	Thr	Ser	Cys	Pro	Arg	Ala	Lys
545					550					555					560

Pro Ser Val Arg Pro Lys Pro Phe Leu Asn Arg Ala Glu Ser Gln Ser  
 565 570 575  
 Gln Glu Lys Met Asp Ile Ser Thr Leu Arg Arg Gln Leu Arg Pro Thr  
 580 585 590  
 Gly Gln Leu Arg Gly Gly Leu Lys Gly Ser Lys Ser Glu Asp Ser Glu  
 595 600 605  
 Leu Pro Pro Gln Thr Ala Ser Glu Ala Pro Ser Glu Gly Ser Arg Arg  
 610 615 620  
 Ser Ser Ser Asp Leu Ile Thr Leu Pro Ala Thr Thr Pro Pro Cys Pro  
 625 630 635 640  
 Thr Lys Lys Glu Trp Glu Gly Pro Ala Thr Ser Tyr Met Thr Cys Ser  
 645 650 655  
 Ala Tyr Gln Lys Val Gln Asp Ser Glu Ile Ser Phe Pro Ala Gly Val  
 660 665 670  
 Glu Val Gln Val Leu Glu Lys Gln Glu Ser Gly Trp Trp Tyr Val Arg  
 675 680 685  
 Phe Gly Glu Leu Glu Gly Trp Ala Pro Ser His Tyr Leu Val Leu Asp  
 690 695 700  
 Glu Asn Glu Gln Pro Asp Pro Ser Gly Lys Glu Leu Asp Thr Val Pro  
 705 710 715 720  
 Ala Lys Gly Arg Gln Asn Glu Gly Lys Ser Asp Ser Leu Glu Lys Ile  
 725 730 735  
 Glu Arg Arg Val Gln Ala Leu Asn Thr Val Asn Gln Ser Lys Lys Ala  
 740 745 750  
 Thr Pro Pro Ile Pro Ser Lys Pro Pro Gly Gly Phe Gly Lys Thr Ser  
 755 760 765  
 Gly Thr Pro Ala Val Lys Met Arg Asn Gly Val Arg Gln Val Ala Val  
 770 775 780  
 Arg Pro Gln Ser Val Phe Val Ser Pro Pro Pro Lys Asp Asn Asn Leu  
 785 790 795 800  
 Ser Cys Ala Leu Arg Arg Asn Glu Ser Leu Thr Ala Thr Asp Gly Leu  
 805 810 815  
 Arg Gly Val Arg Arg Asn Ser Ser Phe Ser Thr Ala Arg Ser Ala Ala  
 820 825 830  
 Ala Glu Ala Lys Gly Arg Leu Ala Glu Arg Ala Ala Ser Gln Gly Ser  
 835 840 845  
 Asp Ser Pro Leu Leu Pro Ala Gln Arg Asn Ser Ile Pro Val Ser Pro  
 850 855 860  
 Val Arg Pro Lys Pro Ile Glu Lys Ser Gln Phe Ile His Asn Asn Leu  
 865 870 875 880  
 Lys Asp Val Tyr Val Ser Ile Ala Asp Tyr Glu Gly Asp Glu Glu Thr  
 885 890 895  
 Ala Gly Phe Gln Glu Gly Val Ser Met Glu Val Leu Glu Arg Asn Pro  
 900 905 910  
 Asn Gly Trp Trp Tyr Cys Gln Ile Leu Asp Gly Val Lys Pro Phe Lys  
 915 920 925  
 Gly Trp Val Pro Ser Asn Tyr Leu Glu Lys Lys Asn  
 930 935 940

&lt;210&gt; 275

&lt;211&gt; 871

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 275

Met Lys Tyr Ser Cys Cys Ala Leu Val Leu Ala Val Leu Gly Thr Glu  
 1 5 10 15

Leu Leu Gly Ser Leu Cys Ser Thr Val Arg Ser Pro Arg Phe Arg Gly  
 20 25 30  
 Arg Ile Gln Glu Arg Lys Asn Ile Arg Pro Asn Ile Ile Leu Val  
 35 40 45  
 Pro Thr Asp Asp Gln Asp Val Glu Leu Gly Ser Leu Gln Val Met Asn  
 50 55 60  
 Lys Thr Arg Lys Ile Met Glu His Gly Gly Ala Thr Phe Ile Asn Ala  
 65 70 75 80  
 Phe Val Thr Thr Pro Met Cys Cys Pro Ser Arg Ser Ser Met Leu Thr  
 85 90 95  
 Gly Lys Tyr Val His Asn His Asn Val Tyr Thr Asn Asn Glu Asn Cys  
 100 105 110  
 Ser Ser Pro Ser Trp Gln Ala Met His Glu Pro Arg Thr Phe Ala Val  
 115 120 125  
 Tyr Leu Asn Asn Thr Gly Tyr Arg Thr Ala Phe Phe Gly Lys Tyr Leu  
 130 135 140  
 Asn Glu Tyr Asn Gly Ser Tyr Ile Pro Pro Gly Trp Arg Glu Trp Leu  
 145 150 155 160  
 Gly Leu Ile Lys Asn Ser Arg Phe Tyr Asn Tyr Thr Val Cys Arg Asn  
 165 170 175  
 Gly Ile Lys Glu Lys His Gly Phe Asp Tyr Ala Lys Asp Tyr Phe Thr  
 180 185 190  
 Asp Leu Ile Thr Asn Glu Ser Ile Asn Tyr Phe Lys Met Ser Lys Arg  
 195 200 205  
 Met Tyr Pro His Arg Pro Val Met Met Val Ile Ser His Ala Ala Pro  
 210 215 220  
 His Gly Pro Glu Asp Ser Ala Pro Gln Phe Ser Lys Leu Tyr Pro Asn  
 225 230 235 240  
 Ala Ser Gln His Ile Thr Pro Ser Tyr Asn Tyr Ala Pro Asn Met Asp  
 245 250 255  
 Lys His Trp Ile Met Gln Tyr Thr Gly Pro Met Leu Pro Ile His Met  
 260 265 270  
 Glu Phe Thr Asn Ile Leu Gln Arg Lys Arg Leu Gln Thr Leu Met Ser  
 275 280 285  
 Val Asp Asp Ser Val Glu Arg Leu Tyr Asn Met Leu Val Glu Thr Gly  
 290 295 300  
 Glu Leu Glu Asn Thr Tyr Ile Ile Tyr Thr Ala Asp His Gly Tyr His  
 305 310 315 320  
 Ile Gly Gln Phe Gly Leu Val Lys Gly Lys Ser Met Pro Tyr Asp Phe  
 325 330 335  
 Asp Ile Arg Val Pro Phe Phe Ile Arg Gly Pro Ser Val Glu Pro Gly  
 340 345 350  
 Ser Ile Val Pro Gln Ile Val Leu Asn Ile Asp Leu Ala Pro Thr Ile  
 355 360 365  
 Leu Asp Ile Ala Gly Leu Asp Thr Pro Pro Asp Val Asp Gly Lys Ser  
 370 375 380  
 Val Leu Lys Leu Leu Asp Pro Glu Lys Pro Gly Asn Arg Phe Arg Thr  
 385 390 395 400  
 Asn Lys Lys Ala Lys Ile Trp Arg Asp Thr Phe Leu Val Glu Arg Gly  
 405 410 415  
 Lys Phe Leu Arg Lys Lys Glu Glu Ser Ser Lys Asn Ile Gln Gln Ser  
 420 425 430  
 Asn His Leu Pro Lys Tyr Glu Arg Val Lys Glu Leu Cys Gln Gln Ala  
 435 440 445  
 Arg Tyr Gln Thr Ala Cys Glu Gln Pro Gly Gln Lys Trp Gln Cys Ile  
 450 455 460  
 Glu Asp Thr Ser Gly Lys Leu Arg Ile His Lys Cys Lys Gly Pro Ser  
 465 470 475 480  
 Asp Leu Leu Thr Val Arg Gln Ser Thr Arg Asn Leu Tyr Ala Arg Gly  
 485 490 495  
 Phe His Asp Lys Asp Lys Glu Cys Ser Cys Arg Glu Ser Gly Tyr Arg  
 500 505 510

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Ala Ser Arg Ser Gln Arg Lys Ser Gln Arg Gln Phe Leu Arg Asn Gln  
 515 520 525  
 Gly Thr Pro Lys Tyr Lys Pro Arg Phe Val His Thr Arg Gln Thr Arg  
 530 535 540  
 Ser Leu Ser Val Glu Phe Glu Gly Glu Ile Tyr Asp Ile Asn Leu Glu  
 545 550 555 560  
 Glu Glu Glu Glu Leu Gln Val Leu Gln Pro Arg Asn Ile Ala Lys Arg  
 565 570 575  
 His Asp Glu Gly His Lys Gly Pro Arg Asp Leu Gln Ala Ser Ser Gly  
 580 585 590  
 Gly Asn Arg Gly Arg Met Leu Ala Asp Ser Ser Asn Ala Val Gly Pro  
 595 600 605  
 Pro Thr Thr Val Arg Val Thr His Lys Cys Phe Ile Leu Pro Asn Asp  
 610 615 620  
 Ser Ile His Cys Glu Arg Glu Leu Tyr Gln Ser Ala Arg Ala Trp Lys  
 625 630 635 640  
 Asp His Lys Ala Tyr Ile Asp Lys Glu Ile Glu Ala Leu Gln Asp Lys  
 645 650 655  
 Ile Lys Asn Leu Arg Glu Val Arg Gly His Leu Lys Arg Arg Lys Pro  
 660 665 670  
 Glu Glu Cys Ser Cys Ser Lys Gln Ser Tyr Tyr Asn Lys Glu Lys Gly  
 675 680 685  
 Val Lys Lys Gln Glu Lys Leu Lys Ser His Leu His Pro Phe Lys Glu  
 690 695 700  
 Ala Ala Gln Glu Val Asp Ser Lys Leu Gln Leu Phe Lys Glu Asn Asn  
 705 710 715 720  
 Arg Arg Arg Lys Lys Glu Arg Lys Glu Lys Arg Arg Gln Arg Lys Gly  
 725 730 735  
 Glu Glu Cys Ser Leu Pro Gly Leu Thr Cys Phe Thr His Asp Asn Asn  
 740 745 750  
 His Trp Gln Thr Ala Pro Phe Trp Asn Leu Gly Ser Phe Cys Ala Cys  
 755 760 765  
 Thr Ser Ser Asn Asn Asn Thr Tyr Trp Cys Leu Arg Thr Val Asn Glu  
 770 775 780  
 Thr His Asn Phe Leu Phe Cys Glu Phe Ala Thr Gly Phe Leu Glu Tyr  
 785 790 795 800  
 Phe Asp Met Asn Thr Asp Pro Tyr Gln Leu Thr Asn Thr Val His Thr  
 805 810 815  
 Val Glu Arg Gly Ile Leu Asn Gln Leu His Val Gln Leu Met Glu Leu  
 820 825 830  
 Arg Ser Cys Gln Gly Tyr Lys Gln Cys Asn Pro Arg Pro Lys Asn Leu  
 835 840 845  
 Asp Val Gly Asn Lys Asp Gly Gly Ser Tyr Asp Leu His Arg Gly Gln  
 850 855 860  
 Leu Trp Asp Gly Trp Glu Gly  
 865 870

&lt;210&gt; 276

&lt;211&gt; 1426

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 276

Met Asn Asp Trp His Arg Ile Phe Thr Gln Asn Val Leu Val Pro Pro  
 1 5 10 15  
 His Pro Gln Arg Ala Arg Gln Pro Trp Lys Glu Ser Thr Ala Phe Gln  
 20 25 30

Cys Val Leu Lys Trp Leu Asp Gly Pro Val Ile Arg Gln Gly Val Leu  
 35 40 45  
 Glu Val Leu Ser Glu Val Glu Cys His Leu Arg Val Ser Phe Phe Asp  
 50 55 60  
 Val Thr Tyr Arg His Phe Phe Gly Arg Thr Trp Lys Thr Thr Val Lys  
 65 70 75 80  
 Pro Thr Lys Arg Pro Pro Ser Arg Ile Val Phe Asn Glu Pro Leu Tyr  
 85 90 95  
 Phe His Thr Ser Leu Asn His Pro His Ile Val Ala Val Val Glu Val  
 100 105 110  
 Val Ala Glu Gly Lys Lys Arg Asp Gly Ser Leu Gln Thr Leu Ser Cys  
 115 120 125  
 Gly Phe Gly Ile Leu Arg Ile Phe Ser Asn Gln Pro Asp Ser Pro Ile  
 130 135 140  
 Ser Ala Ser Gln Asp Lys Arg Leu Arg Leu Tyr His Gly Thr Pro Arg  
 145 150 155 160  
 Ala Leu Leu His Pro Leu Leu Gln Asp Pro Ala Glu Gln Asn Arg His  
 165 170 175  
 Met Thr Leu Ile Glu Asn Cys Ser Leu Gln Tyr Thr Leu Lys Pro His  
 180 185 190  
 Pro Ala Leu Glu Pro Ala Phe His Leu Leu Pro Glu Asn Leu Leu Val  
 195 200 205  
 Ser Gly Leu Gln Gln Ile Pro Gly Leu Leu Pro Ala His Gly Glu Ser  
 210 215 220  
 Gly Asp Ala Leu Arg Lys Pro Arg Leu Gln Lys Pro Ile Thr Gly His  
 225 230 235 240  
 Leu Asp Asp Leu Phe Phe Thr Leu Tyr Pro Ser Leu Glu Lys Phe Glu  
 245 250 255  
 Glu Glu Leu Leu Glu Leu His Val Gln Asp His Phe Gln Glu Gly Cys  
 260 265 270  
 Gly Pro Leu Asp Gly Gly Ala Leu Glu Ile Leu Glu Arg Arg Leu Arg  
 275 280 285  
 Val Gly Val His Asn Gly Leu Gly Phe Val Gln Arg Pro Gln Val Val  
 290 295 300  
 Val Leu Val Pro Glu Met Asp Val Ala Leu Thr Arg Ser Ala Ser Phe  
 305 310 315 320  
 Ser Arg Lys Val Val Ser Ser Ser Lys Thr Ser Ser Gly Ser Gln Ala  
 325 330 335  
 Leu Val Leu Arg Ser Arg Leu Arg Leu Pro Glu Met Val Gly His Pro  
 340 345 350  
 Ala Phe Ala Val Ile Phe Gln Leu Glu Tyr Val Phe Ser Ser Pro Ala  
 355 360 365  
 Gly Val Asp Gly Asn Ala Ala Ser Val Thr Ser Leu Ser Asn Leu Ala  
 370 375 380  
 Cys Met His Met Val Arg Trp Ala Val Trp Asn Pro Leu Leu Glu Ala  
 385 390 395 400  
 Asp Ser Gly Arg Val Thr Leu Pro Leu Gln Gly Gly Ile Gln Pro Asn  
 405 410 415  
 Pro Ser His Cys Leu Val Tyr Lys Val Pro Ser Ala Ser Met Ser Ser  
 420 425 430  
 Glu Glu Val Lys Gln Val Glu Ser Gly Thr Leu Arg Phe Gln Phe Ser  
 435 440 445  
 Leu Gly Ser Glu Glu His Leu Asp Ala Pro Thr Glu Pro Val Ser Gly  
 450 455 460  
 Pro Lys Val Glu Arg Arg Pro Ser Arg Lys Pro Pro Thr Ser Pro Ser  
 465 470 475 480  
 Ser Pro Pro Ala Pro Val Pro Arg Val Leu Ala Ala Pro Gln Asn Ser  
 485 490 495  
 Pro Val Gly Pro Gly Leu Ser Ile Ser Gln Leu Ala Ala Ser Pro Arg  
 500 505 510  
 Ser Pro Thr Gln His Cys Leu Ala Arg Pro Thr Ser Gln Leu Pro His  
 515 520 525



Gly Ser Gln Ala Ser Pro Ala Gln Ala Gln Glu Phe Pro Leu Glu Ala  
 530 535 540  
 Gly Ile Ser His Leu Glu Ala Asp Leu Ser Gln Thr Ser Leu Val Leu  
 545 550 555 560  
 Glu Thr Ser Ile Ala Glu Gln Leu Gln Glu Leu Pro Phe Thr Pro Leu  
 565 570 575  
 His Ala Pro Ile Val Val Gly Thr Gln Thr Arg Ser Ser Ala Gly Gln  
 580 585 590  
 Pro Ser Arg Ala Ser Met Val Leu Leu Gln Ser Ser Gly Phe Pro Glu  
 595 600 605  
 Ile Leu Asp Ala Asn Lys Gln Pro Ala Glu Ala Val Ser Ala Thr Glu  
 610 615 620  
 Pro Val Thr Phe Asn Pro Gln Lys Glu Glu Ser Asp Cys Leu Gln Ser  
 625 630 635 640  
 Asn Glu Met Val Leu Gln Phe Leu Ala Phe Ser Arg Val Ala Gln Asp  
 645 650 655  
 Cys Arg Gly Thr Ser Trp Pro Lys Thr Val Tyr Phe Thr Phe Gln Phe  
 660 665 670  
 Tyr Arg Phe Pro Pro Ala Thr Thr Pro Arg Leu Gln Leu Val Gln Leu  
 675 680 685  
 Asp Glu Ala Gly Gln Pro Ser Ser Gly Ala Leu Thr His Ile Leu Val  
 690 695 700  
 Pro Val Ser Arg Asp Gly Thr Phe Asp Ala Gly Ser Pro Gly Phe Gln  
 705 710 715 720  
 Leu Arg Tyr Met Val Gly Pro Gly Phe Leu Lys Pro Gly Glu Arg Arg  
 725 730 735  
 Cys Phe Ala Arg Tyr Leu Ala Val Gln Thr Leu Gln Ile Asp Val Trp  
 740 745 750  
 Asp Gly Asp Ser Leu Leu Leu Ile Gly Ser Ala Ala Val Gln Met Lys  
 755 760 765  
 His Leu Leu Arg Gln Gly Arg Pro Ala Val Gln Ala Ser His Glu Leu  
 770 775 780  
 Glu Val Val Ala Thr Glu Tyr Glu Gln Asp Asn Met Val Val Ser Gly  
 785 790 795 800  
 Asp Met Leu Gly Phe Gly Arg Val Lys Pro Ile Gly Val His Ser Val  
 805 810 815  
 Val Lys Gly Arg Leu His Leu Thr Leu Ala Asn Val Gly His Pro Cys  
 820 825 830  
 Glu Gln Lys Val Arg Gly Cys Ser Thr Leu Pro Pro Ser Arg Ser Arg  
 835 840 845  
 Val Ile Ser Asn Asp Gly Ala Ser Arg Phe Ser Gly Gly Ser Leu Leu  
 850 855 860  
 Thr Thr Gly Ser Ser Arg Arg Lys His Val Val Gln Ala Gln Lys Leu  
 865 870 875 880  
 Ala Asp Val Asp Ser Glu Leu Ala Ala Met Leu Leu Thr His Ala Arg  
 885 890 895  
 Gln Gly Lys Gly Pro Gln Asp Val Ser Arg Glu Ser Asp Ala Thr Arg  
 900 905 910  
 Arg Arg Lys Leu Glu Arg Met Arg Ser Val Arg Leu Gln Glu Ala Gly  
 915 920 925  
 Gly Asp Leu Gly Arg Arg Gly Thr Ser Val Leu Ala Gln Gln Ser Val  
 930 935 940  
 Arg Thr Gln His Leu Arg Asp Leu Gln Val Ile Ala Ala Tyr Arg Glu  
 945 950 955 960  
 Arg Thr Lys Ala Glu Ser Ile Ala Ser Leu Leu Ser Leu Ala Ile Thr  
 965 970 975  
 Thr Glu His Thr Leu His Ala Thr Leu Gly Val Ala Glu Phe Phe Glu  
 980 985 990  
 Phe Val Leu Lys Asn Pro His Asn Thr Gln His Thr Val Thr Val Glu  
 995 1000 1005  
 Ile Asp Asn Pro Glu Leu Ser Val Ile Val Asp Ser Gln Glu Trp  
 1010 1015 1020

Arg	Asp	Phe	Lys	Gly	Ala	Ala	Gly	Leu	His	Thr	Pro	Val	Glu	Glu
1025						1030					1035			
Asp	Met	Phe	His	Leu	Arg	Gly	Ser	Leu	Ala	Pro	Gln	Leu	Tyr	Leu
1040						1045					1050			
Arg	Pro	His	Glu	Thr	Ala	His	Val	Pro	Phe	Lys	Phe	Gln	Ser	Phe
1055						1060					1065			
Ser	Ala	Gly	Gln	Leu	Ala	Met	Val	Gln	Ala	Ser	Pro	Gly	Leu	Ser
1070						1075					1080			
Asn	Glu	Lys	Gly	Met	Asp	Ala	Val	Ser	Pro	Trp	Lys	Ser	Ser	Ala
1085						1090					1095			
Val	Pro	Thr	Lys	His	Ala	Lys	Val	Leu	Phe	Arg	Ala	Ser	Gly	Gly
1100						1105					1110			
Lys	Pro	Ile	Ala	Val	Leu	Cys	Leu	Thr	Val	Glu	Leu	Gln	Pro	His
1115						1120					1125			
Val	Val	Asp	Gln	Val	Phe	Arg	Phe	Tyr	His	Pro	Glu	Leu	Ser	Phe
1130						1135					1140			
Leu	Lys	Lys	Ala	Ile	Arg	Leu	Pro	Pro	Trp	His	Thr	Phe	Pro	Gly
1145						1150					1155			
Ala	Pro	Val	Gly	Met	Leu	Gly	Glu	Asp	Pro	Pro	Val	His	Val	Arg
1160						1165					1170			
Cys	Ser	Asp	Pro	Asn	Val	Ile	Cys	Glu	Thr	Gln	Asn	Val	Gly	Pro
1175						1180					1185			
Gly	Glu	Pro	Arg	Asp	Ile	Phe	Leu	Lys	Val	Ala	Ser	Gly	Pro	Ser
1190						1195					1200			
Pro	Glu	Ile	Lys	Asp	Phe	Phe	Val	Ile	Ile	Tyr	Ser	Asp	Arg	Trp
1205						1210					1215			
Leu	Ala	Thr	Pro	Thr	Gln	Thr	Trp	Gln	Val	Tyr	Leu	His	Ser	Leu
1220						1225					1230			
Gln	Arg	Val	Asp	Val	Ser	Cys	Val	Ala	Gly	Gln	Leu	Thr	Arg	Leu
1235						1240					1245			
Ser	Leu	Val	Leu	Arg	Gly	Thr	Gln	Thr	Val	Arg	Lys	Val	Arg	Ala
1250						1255					1260			
Phe	Thr	Ser	His	Pro	Gln	Glu	Leu	Lys	Thr	Asp	Pro	Lys	Gly	Val
1265						1270					1275			
Phe	Val	Leu	Pro	Pro	Arg	Gly	Val	Gln	Asp	Leu	His	Val	Gly	Val
1280						1285					1290			
Arg	Pro	Leu	Arg	Ala	Gly	Ser	Arg	Phe	Val	His	Leu	Asn	Leu	Val
1295						1300					1305			
Asp	Val	Asp	Cys	His	Gln	Leu	Val	Ala	Ser	Trp	Leu	Val	Cys	Leu
1310						1315					1320			
Cys	Cys	Arg	Gln	Pro	Leu	Ile	Ser	Lys	Ala	Phe	Glu	Ile	Met	Leu
1325						1330					1335			
Ala	Ala	Gly	Glu	Gly	Lys	Gly	Val	Asn	Lys	Arg	Ile	Thr	Tyr	Thr
1340						1345					1350			
Asn	Pro	Tyr	Pro	Ser	Arg	Arg	Thr	Phe	His	Leu	His	Ser	Asp	His
1355						1360					1365			
Pro	Glu	Leu	Leu	Arg	Phe	Arg	Glu	Asp	Ser	Phe	Gln	Val	Gly	Gly
1370						1375					1380			
Gly	Glu	Thr	Tyr	Thr	Ile	Gly	Leu	Gln	Phe	Ala	Pro	Ser	Gln	Arg
1385						1390					1395			
Val	Gly	Glu	Glu	Glu	Ile	Leu	Ile	Tyr	Ile	Asn	Asp	His	Glu	Asp
1400						1405					1410			
Lys	Asn	Glu	Glu	Ala	Phe	Cys	Val	Lys	Val	Ile	Tyr	Gln		
1415						1420					1425			

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&lt;210&gt; 277

&lt;211&gt; 146

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 277

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Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg Ser Met Pro Leu Gly
1      5      10      15
Val Arg Ile Leu Phe His Gly Val Phe Tyr Ala Gly Gly Phe Ala Ile
20      25      30
Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg Ala Leu Tyr Tyr Lys
35      40      45
Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu Ala Gln Glu Ala Leu
50      55      60
Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu Ile Asp Arg Glu Asn
65      70      75      80
Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile Pro Val Ser Gly Ser
85      90      95
Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser Arg Gly Gly Pro Phe
100     105     110
Gln Arg Trp His Leu Asp Glu Val Phe Leu Glu Leu Lys Asp Gly Gln
115     120     125
Gln Ile Pro Val Phe Lys Leu Ser Gly Glu Asn Gly Asp Glu Val Lys
130     135     140
Lys Glu
145

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&lt;210&gt; 278

&lt;211&gt; 402

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 278

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Met Lys Glu Thr Arg Gly Tyr Gly Gly Asp Ala Pro Phe Cys Thr Arg
1      5      10      15
Leu Asn His Ser Tyr Thr Gly Met Trp Ala Pro Glu Arg Ser Ala Glu
20      25      30
Ala Arg Gly Asn Leu Thr Arg Pro Pro Gly Ser Gly Glu Asp Cys Gly
35      40      45
Ser Val Ser Val Ala Phe Pro Ile Thr Met Leu Leu Thr Gly Phe Val
50      55      60
Gly Asn Ala Leu Ala Met Leu Leu Val Ser Arg Ser Tyr Arg Arg Arg
65      70      75      80
Glu Ser Lys Arg Lys Lys Ser Phe Leu Leu Cys Ile Gly Trp Leu Ala
85      90      95
Leu Thr Asp Leu Val Gly Gln Leu Leu Thr Thr Pro Val Val Ile Val
100     105     110
Val Tyr Leu Ser Lys Gln Arg Trp Glu His Ile Asp Pro Ser Gly Arg
115     120     125
Leu Cys Thr Phe Phe Gly Leu Thr Met Thr Val Phe Gly Leu Ser Ser
130     135     140

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Leu Phe Ile Ala Ser Ala Met Ala Val Glu Arg Ala Leu Ala Ile Arg  
 145 150 155 160  
 Ala Pro His Trp Tyr Ala Ser His Met Lys Thr Arg Ala Thr Arg Ala  
 165 170 175  
 Val Leu Leu Gly Val Trp Leu Ala Val Leu Ala Phe Ala Leu Leu Pro  
 180 185 190  
 Val Leu Gly Val Gly Gln Tyr Thr Val Gln Trp Pro Gly Thr Trp Cys  
 195 200 205  
 Phe Ile Ser Thr Gly Arg Gly Gly Asn Gly Thr Ser Ser Ser His Asn  
 210 215 220  
 Trp Gly Asn Leu Phe Phe Ala Ser Ala Phe Ala Phe Leu Gly Leu Leu  
 225 230 235 240  
 Ala Leu Thr Val Thr Phe Ser Cys Asn Leu Ala Thr Ile Lys Ala Leu  
 245 250 255  
 Val Ser Arg Cys Arg Ala Lys Ala Thr Ala Ser Gln Ser Ser Ala Gln  
 260 265 270  
 Trp Gly Arg Ile Thr Thr Glu Thr Ala Ile Gln Leu Met Gly Ile Met  
 275 280 285  
 Cys Val Leu Ser Val Cys Trp Ser Pro Leu Leu Ile Met Met Leu Lys  
 290 295 300  
 Met Ile Phe Asn Gln Thr Ser Val Glu His Cys Lys Thr His Thr Glu  
 305 310 315 320  
 Lys Gln Lys Glu Cys Asn Phe Phe Leu Ile Ala Val Arg Leu Ala Ser  
 325 330 335  
 Leu Asn Gln Ile Leu Asp Pro Trp Val Tyr Leu Leu Leu Arg Lys Ile  
 340 345 350  
 Leu Leu Arg Lys Phe Cys Gln Met Arg Lys Arg Arg Leu Arg Glu Gln  
 355 360 365  
 Glu Met Gly Pro Asp Gly Arg Cys Phe Cys His Ala Trp Arg Gln Val  
 370 375 380  
 Pro Arg Thr Trp Cys Ser Ser His Asp Arg Glu Pro Cys Ser Val Gln  
 385 390 395 400  
 Leu Ser

&lt;210&gt; 279

&lt;211&gt; 1741

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 279

Met Arg Leu Leu Trp Gly Leu Ile Trp Ala Ser Ser Phe Phe Thr Leu  
 1 5 10 15  
 Ser Leu Gln Lys Pro Arg Leu Leu Leu Phe Ser Pro Ser Val Val His  
 20 25 30  
 Leu Gly Val Pro Leu Ser Val Gly Val Gln Leu Gln Asp Val Pro Arg  
 35 40 45  
 Gly Gln Val Val Lys Gly Ser Val Phe Leu Arg Asn Pro Ser Arg Asn  
 50 55 60  
 Asn Val Pro Cys Ser Pro Lys Val Asp Phe Thr Leu Ser Ser Glu Arg  
 65 70 75 80  
 Asp Phe Ala Leu Leu Ser Leu Gln Val Pro Leu Lys Asp Ala Lys Ser  
 85 90 95  
 Cys Gly Leu His Gln Leu Leu Arg Gly Pro Glu Val Gln Leu Val Ala  
 100 105 110  
 His Ser Pro Trp Leu Lys Asp Ser Leu Ser Arg Thr Thr Asn Ile Gln  
 115 120 125

Gly Ile Asn Leu Leu Phe Ser Ser Arg Arg Gly His Leu Phe Leu Gln  
 130 135 140  
 Thr Asp Gln Pro Ile Tyr Asn Pro Gly Gln Arg Val Arg Tyr Arg Val  
 145 150 155 160  
 Phe Ala Leu Asp Gln Lys Met Arg Pro Ser Thr Asp Thr Ile Thr Val  
 165 170 175  
 Met Val Glu Asn Ser His Gly Leu Arg Val Arg Lys Lys Glu Val Tyr  
 180 185 190  
 Met Pro Ser Ser Ile Phe Gln Asp Asp Phe Val Ile Pro Asp Ile Ser  
 195 200 205  
 Glu Pro Gly Thr Trp Lys Ile Ser Ala Arg Phe Ser Asp Gly Leu Glu  
 210 215 220  
 Ser Asn Ser Ser Thr Gln Phe Glu Val Lys Lys Tyr Val Leu Pro Asn  
 225 230 235 240  
 Phe Glu Val Lys Ile Thr Pro Gly Lys Pro Tyr Ile Leu Thr Val Pro  
 245 250 255  
 Gly His Leu Asp Glu Met Gln Leu Asp Ile Gln Ala Arg Tyr Ile Tyr  
 260 265 270  
 Gly Lys Pro Val Gln Gly Val Ala Tyr Val Arg Phe Gly Leu Leu Asp  
 275 280 285  
 Glu Asp Gly Lys Lys Thr Phe Phe Arg Gly Leu Glu Ser Gln Thr Lys  
 290 295 300  
 Leu Val Asn Gly Gln Ser His Ile Ser Leu Ser Lys Ala Glu Phe Gln  
 305 310 315 320  
 Asp Ala Leu Glu Lys Leu Asn Met Gly Ile Thr Asp Leu Gln Gly Leu  
 325 330 335  
 Arg Leu Tyr Val Ala Ala Ala Ile Ile Glu Ser Pro Gly Gly Glu Met  
 340 345 350  
 Glu Glu Ala Glu Leu Thr Ser Trp Tyr Phe Val Ser Ser Pro Phe Ser  
 355 360 365  
 Leu Asp Leu Ser Lys Thr Lys Arg His Leu Val Pro Gly Ala Pro Phe  
 370 375 380  
 Leu Leu Gln Ala Leu Val Arg Glu Met Ser Gly Ser Pro Ala Ser Gly  
 385 390 395 400  
 Ile Pro Val Lys Val Ser Ala Thr Val Ser Ser Pro Gly Ser Val Pro  
 405 410 415  
 Glu Ala Gln Asp Ile Gln Gln Asn Thr Asp Gly Ser Gly Gln Val Ser  
 420 425 430  
 Ile Pro Ile Ile Ile Pro Gln Thr Ile Ser Glu Leu Gln Leu Ser Val  
 435 440 445  
 Ser Ala Gly Ser Pro His Pro Ala Ile Ala Arg Leu Thr Val Ala Ala  
 450 455 460  
 Pro Pro Ser Gly Gly Pro Gly Phe Leu Ser Ile Glu Arg Pro Asp Ser  
 465 470 475 480  
 Arg Pro Pro Arg Val Gly Asp Thr Leu Asn Leu Asn Leu Arg Ala Val  
 485 490 495  
 Gly Ser Gly Ala Thr Phe Ser His Tyr Tyr Tyr Met Ile Leu Ser Arg  
 500 505 510  
 Gly Gln Ile Val Phe Met Asn Arg Glu Pro Lys Arg Thr Leu Thr Ser  
 515 520 525  
 Val Ser Val Phe Val Asp His His Leu Ala Pro Ser Phe Tyr Phe Val  
 530 535 540  
 Ala Phe Tyr Tyr His Gly Asp His Pro Val Ala Asn Ser Leu Arg Val  
 545 550 555 560  
 Asp Val Gln Ala Gly Ala Cys Glu Gly Lys Leu Glu Leu Ser Val Asp  
 565 570 575  
 Gly Ala Lys Gln Tyr Arg Asn Gly Glu Ser Val Lys Leu His Leu Glu  
 580 585 590  
 Thr Asp Ser Leu Ala Leu Val Ala Leu Gly Ala Leu Asp Thr Ala Leu  
 595 600 605  
 Tyr Ala Ala Gly Ser Lys Ser His Lys Pro Leu Asn Met Gly Lys Val  
 610 615 620

Phe	Glu	Ala	Met	Asn	Ser	Tyr	Asp	Leu	Gly	Cys	Gly	Pro	Gly	Gly	Gly
625					630					635					640
Asp	Ser	Ala	Leu	Gln	Val	Phe	Gln	Ala	Ala	Gly	Leu	Ala	Phe	Ser	Asp
				645					650					655	
Gly	Asp	Gln	Trp	Thr	Leu	Ser	Arg	Lys	Arg	Leu	Ser	Cys	Pro	Lys	Glu
			660					665					670		
Lys	Thr	Thr	Arg	Lys	Lys	Arg	Asn	Val	Asn	Phe	Gln	Lys	Ala	Ile	Asn
			675				680					685			
Glu	Lys	Leu	Gly	Gln	Tyr	Ala	Ser	Pro	Thr	Ala	Lys	Arg	Cys	Cys	Gln
	690					695					700				
Asp	Gly	Val	Thr	Arg	Leu	Pro	Met	Met	Arg	Ser	Cys	Glu	Gln	Arg	Ala
705					710					715					720
Ala	Arg	Val	Gln	Gln	Pro	Asp	Cys	Arg	Glu	Pro	Phe	Leu	Ser	Cys	Cys
				725					730					735	
Gln	Phe	Ala	Glu	Ser	Leu	Arg	Lys	Lys	Ser	Arg	Asp	Lys	Gly	Gln	Ala
			740					745					750		
Gly	Leu	Gln	Arg	Ala	Leu	Glu	Ile	Leu	Gln	Glu	Glu	Asp	Leu	Ile	Asp
		755					760					765			
Glu	Asp	Asp	Ile	Pro	Val	Arg	Ser	Phe	Phe	Pro	Glu	Asn	Trp	Leu	Trp
	770					775					780				
Arg	Val	Glu	Thr	Val	Asp	Arg	Phe	Gln	Ile	Leu	Thr	Leu	Trp	Leu	Pro
785					790					795					800
Asp	Ser	Leu	Thr	Thr	Trp	Glu	Ile	His	Gly	Leu	Ser	Leu	Ser	Lys	Thr
				805					810					815	
Lys	Gly	Leu	Cys	Val	Ala	Thr	Pro	Val	Gln	Leu	Arg	Val	Phe	Arg	Glu
			820					825					830		
Phe	His	Leu	His	Leu	Arg	Leu	Pro	Met	Ser	Val	Arg	Arg	Phe	Glu	Gln
		835					840					845			
Leu	Glu	Leu	Arg	Pro	Val	Leu	Tyr	Asn	Tyr	Leu	Asp	Lys	Asn	Leu	Thr
	850					855					860				
Val	Ser	Val	His	Val	Ser	Pro	Val	Glu	Gly	Leu	Cys	Leu	Ala	Gly	Gly
865					870					875					880
Gly	Gly	Leu	Ala	Gln	Gln	Val	Leu	Val	Pro	Ala	Gly	Ser	Ala	Arg	Pro
				885					890					895	
Val	Ala	Phe	Ser	Val	Val	Pro	Thr	Ala	Ala	Ala	Ala	Val	Ser	Leu	Lys
			900					905					910		
Val	Val	Ala	Arg	Gly	Ser	Phe	Glu	Phe	Pro	Val	Gly	Asp	Ala	Val	Ser
		915					920					925			
Lys	Val	Leu	Gln	Ile	Glu	Lys	Glu	Gly	Ala	Ile	His	Arg	Glu	Glu	Leu
	930					935					940				
Val	Tyr	Glu	Leu	Asn	Pro	Leu	Asp	His	Arg	Gly	Arg	Thr	Leu	Glu	Ile
945					950					955					960
Pro	Gly	Asn	Ser	Asp	Pro	Asn	Met	Ile	Pro	Asp	Gly	Asp	Phe	Asn	Ser
				965					970					975	
Tyr	Val	Arg	Val	Thr	Ala	Ser	Asp	Pro	Leu	Asp	Thr	Leu	Gly	Ser	Glu
			980					985					990		
Gly	Ala	Leu	Ser	Pro	Gly	Gly	Val	Ala	Ser	Leu	Leu	Arg	Leu	Pro	Arg
		995					1000					1005			
Gly	Cys	Gly	Glu	Gln	Thr	Met	Ile	Tyr	Leu	Ala	Pro	Thr	Leu	Ala	
	1010					1015					1020				
Ala	Ser	Arg	Tyr	Leu	Asp	Lys	Thr	Glu	Gln	Trp	Ser	Thr	Leu	Pro	
	1025					1030					1035				
Pro	Glu	Thr	Lys	Asp	His	Ala	Val	Asp	Leu	Ile	Gln	Lys	Gly	Tyr	
	1040					1045					1050				
Met	Arg	Ile	Gln	Gln	Phe	Arg	Lys	Ala	Asp	Gly	Ser	Tyr	Ala	Ala	
	1055					1060					1065				
Trp	Leu	Ser	Arg	Asp	Ser	Ser	Thr	Trp	Leu	Thr	Ala	Phe	Val	Leu	
	1070					1075					1080				
Lys	Val	Leu	Ser	Leu	Ala	Gln	Glu	Gln	Val	Gly	Gly	Ser	Pro	Glu	
	1085					1090					1095				
Lys	Leu	Gln	Glu	Thr	Ser	Asn	Trp	Leu	Leu	Ser	Gln	Gln	Gln	Ala	
	1100					1105					1110				

Asp	Gly	Ser	Phe	Gln	Asp	Pro	Cys	Pro	Val	Leu	Asp	Arg	Ser	Met
1115						1120					1125			
Gln	Gly	Gly	Leu	Val	Gly	Asn	Asp	Glu	Thr	Val	Ala	Leu	Thr	Ala
1130						1135					1140			
Phe	Val	Thr	Ile	Ala	Leu	His	His	Gly	Leu	Ala	Val	Phe	Gln	Asp
1145						1150					1155			
Glu	Gly	Ala	Glu	Pro	Leu	Lys	Gln	Arg	Val	Glu	Ala	Ser	Ile	Ser
1160						1165					1170			
Lys	Ala	Asn	Ser	Phe	Leu	Gly	Glu	Lys	Ala	Ser	Ala	Gly	Leu	Leu
1175						1180					1185			
Gly	Ala	His	Ala	Ala	Ala	Ile	Thr	Ala	Tyr	Ala	Leu	Ser	Leu	Thr
1190						1195					1200			
Lys	Ala	Pro	Val	Asp	Leu	Leu	Gly	Val	Ala	His	Asn	Asn	Leu	Met
1205						1210					1215			
Ala	Met	Ala	Gln	Glu	Thr	Gly	Asp	Asn	Leu	Tyr	Trp	Gly	Ser	Val
1220						1225					1230			
Thr	Gly	Ser	Gln	Ser	Asn	Ala	Val	Ser	Pro	Thr	Pro	Ala	Pro	Arg
1235						1240					1245			
Asn	Pro	Ser	Asp	Pro	Met	Pro	Gln	Ala	Pro	Ala	Leu	Trp	Ile	Glu
1250						1255					1260			
Thr	Thr	Ala	Tyr	Ala	Leu	Leu	His	Leu	Leu	Leu	His	Glu	Gly	Lys
1265						1270					1275			
Ala	Glu	Met	Ala	Asp	Gln	Ala	Ser	Ala	Trp	Leu	Thr	Arg	Gln	Gly
1280						1285					1290			
Ser	Phe	Gln	Gly	Gly	Phe	Arg	Ser	Thr	Gln	Asp	Thr	Val	Ile	Ala
1295						1300					1305			
Leu	Asp	Ala	Leu	Ser	Ala	Tyr	Trp	Ile	Ala	Ser	His	Thr	Thr	Glu
1310						1315					1320			
Glu	Arg	Gly	Leu	Asn	Val	Thr	Leu	Ser	Ser	Thr	Gly	Arg	Asn	Gly
1325						1330					1335			
Phe	Lys	Ser	His	Ala	Leu	Gln	Leu	Asn	Asn	Arg	Gln	Ile	Arg	Gly
1340						1345					1350			
Leu	Glu	Glu	Glu	Leu	Gln	Phe	Ser	Leu	Gly	Ser	Lys	Ile	Asn	Val
1355						1360					1365			
Lys	Val	Gly	Gly	Asn	Ser	Lys	Gly	Thr	Leu	Lys	Val	Leu	Arg	Thr
1370						1375					1380			
Tyr	Asn	Val	Leu	Asp	Met	Lys	Asn	Thr	Thr	Cys	Gln	Asp	Leu	Gln
1385						1390					1395			
Ile	Glu	Val	Thr	Val	Lys	Gly	His	Val	Glu	Tyr	Thr	Met	Glu	Ala
1400						1405					1410			
Asn	Glu	Asp	Tyr	Glu	Tyr	Asp	Glu	Leu	Pro	Ala	Lys	Asp	Asp	Pro
1415						1420					1425			
Asp	Ala	Pro	Leu	Gln	Pro	Val	Thr	Pro	Leu	Gln	Leu	Phe	Glu	Gly
1430						1435					1440			
Arg	Arg	Asn	Arg	Arg	Arg	Arg	Glu	Ala	Pro	Lys	Val	Val	Glu	Glu
1445						1450					1455			
Gln	Glu	Ser	Arg	Val	His	Tyr	Thr	Val	Cys	Ile	Trp	Arg	Asn	Gly
1460						1465					1470			
Lys	Val	Gly	Leu	Ser	Gly	Met	Ala	Ile	Ala	Asp	Val	Thr	Leu	Leu
1475						1480					1485			
Ser	Gly	Phe	His	Ala	Leu	Arg	Ala	Asp	Leu	Glu	Lys	Leu	Thr	Ser
1490						1495					1500			
Leu	Ser	Asp	Arg	Tyr	Val	Ser	His	Phe	Glu	Thr	Glu	Gly	Pro	His
1505						1510					1515			
Val	Leu	Leu	Tyr	Phe	Asp	Ser	Val	Pro	Thr	Ser	Arg	Glu	Cys	Val
1520						1525					1530			
Gly	Phe	Glu	Ala	Val	Gln	Glu	Val	Pro	Val	Gly	Leu	Val	Gln	Pro
1535						1540					1545			
Ala	Ser	Ala	Thr	Leu	Tyr	Asp	Tyr	Tyr	Asn	Pro	Glu	Arg	Arg	Cys
1550						1555					1560			
Ser	Val	Phe	Tyr	Gly	Ala	Pro	Ser	Lys	Ser	Arg	Leu	Leu	Ala	Thr
1565						1570					1575			

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Leu	Cys	Ser	Ala	Glu	Val	Cys	Gln	Cys	Ala	Glu	Gly	Lys	Cys	Pro
1580						1585					1590			
Arg	Gln	Arg	Arg	Ala	Leu	Glu	Arg	Gly	Leu	Gln	Asp	Glu	Asp	Gly
1595						1600					1605			
Tyr	Arg	Met	Lys	Phe	Ala	Cys	Tyr	Tyr	Pro	Arg	Val	Glu	Tyr	Gly
1610						1615					1620			
Phe	Gln	Val	Lys	Val	Leu	Arg	Glu	Asp	Ser	Arg	Ala	Ala	Phe	Arg
1625						1630					1635			
Leu	Phe	Glu	Thr	Lys	Ile	Thr	Gln	Val	Leu	His	Phe	Thr	Lys	Asp
1640						1645					1650			
Val	Lys	Ala	Ala	Ala	Asn	Gln	Met	Arg	Asn	Phe	Leu	Val	Arg	Ala
1655						1660					1665			
Ser	Cys	Arg	Leu	Arg	Leu	Glu	Pro	Gly	Lys	Glu	Tyr	Leu	Ile	Met
1670						1675					1680			
Gly	Leu	Asp	Gly	Ala	Thr	Tyr	Asp	Leu	Glu	Gly	His	Pro	Gln	Tyr
1685						1690					1695			
Leu	Leu	Asp	Ser	Asn	Ser	Trp	Ile	Glu	Glu	Met	Pro	Ser	Glu	Arg
1700						1705					1710			
Leu	Cys	Arg	Ser	Thr	Arg	Gln	Arg	Ala	Ala	Cys	Ala	Gln	Leu	Asn
1715						1720					1725			
Asp	Phe	Leu	Gln	Glu	Tyr	Gly	Thr	Gln	Gly	Cys	Gln	Val		
1730						1735					1740			

&lt;210&gt; 280

&lt;211&gt; 2150

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 280

Met	Tyr	Pro	Asn	Trp	Gly	Arg	Tyr	Gly	Gly	Ser	Ser	His	Tyr	Pro	Pro
1			5					10						15	
Pro	Pro	Val	Pro	Pro	Pro	Pro	Pro	Val	Ala	Leu	Pro	Glu	Ala	Ser	Pro
			20					25					30		
Gly	Pro	Gly	Tyr	Ser	Ser	Ser	Thr	Thr	Pro	Ala	Ala	Pro	Ser	Ser	Ser
			35				40					45			
Gly	Phe	Met	Ser	Phe	Arg	Glu	Gln	His	Leu	Ala	Gln	Leu	Gln	Gln	Leu
			50			55					60				
Gln	Gln	Met	His	Gln	Lys	Gln	Met	Gln	Cys	Val	Leu	Gln	Pro	His	His
65					70					75				80	
Leu	Pro	Pro	Pro	Pro	Leu	Pro	Pro	Pro	Pro	Val	Met	Pro	Gly	Gly	Gly
					85					90				95	
Tyr	Gly	Asp	Trp	Gln	Pro	Pro	Pro	Pro	Pro	Met	Pro	Pro	Pro	Pro	Gly
			100					105					110		
Pro	Ala	Leu	Ser	Tyr	Gln	Lys	Gln	Gln	Gln	Tyr	Lys	His	Gln	Met	Leu
			115				120					125			
His	His	Gln	Arg	Asp	Gly	Pro	Pro	Gly	Leu	Val	Pro	Met	Glu	Leu	Glu
			130			135					140				
Ser	Pro	Pro	Glu	Ser	Pro	Pro	Val	Pro	Pro	Gly	Ser	Tyr	Met	Pro	Pro
145					150					155				160	
Ser	Gln	Ser	Tyr	Met	Pro	Pro	Pro	Gln	Pro	Pro	Pro	Ser	Tyr	Tyr	Pro
				165						170				175	
Pro	Thr	Ser	Ser	Gln	Pro	Tyr	Leu	Pro	Pro	Ala	Gln	Pro	Ser	Pro	Ser
				180				185					190		
Gln	Ser	Pro	Pro	Ser	Gln	Ser	Tyr	Leu	Ala	Pro	Thr	Pro	Ser	Tyr	Ser
			195				200					205			
Ser	Ser	Ser	Ser	Ser	Ser	Gln	Ser	Tyr	Leu	Ser	His	Ser	Gln	Ser	Tyr
210						215						220			



Leu Pro Ser Ser Gln Ala Ser Pro Ser Arg Pro Ser Gln Gly His Ser  
 225 230 235 240  
 Lys Ser Gln Leu Leu Ala Pro Pro Pro Pro Ser Ala Pro Pro Gly Asn  
 245 250 255  
 Lys Thr Thr Val Gln Gln Glu Pro Leu Glu Ser Gly Ala Lys Asn Lys  
 260 265 270  
 Ser Thr Glu Gln Gln Gln Ala Ala Pro Glu Pro Asp Pro Ser Thr Met  
 275 280 285  
 Thr Pro Gln Glu Gln Gln Gln Tyr Trp Tyr Arg Gln His Leu Leu Ser  
 290 295 300  
 Leu Gln Gln Arg Thr Lys Val His Leu Pro Gly His Lys Lys Gly Pro  
 305 310 315 320  
 Val Val Ala Lys Asp Thr Pro Glu Pro Val Lys Glu Glu Val Thr Val  
 325 330 335  
 Pro Ala Thr Ser Gln Val Pro Glu Ser Pro Ser Ser Glu Glu Pro Pro  
 340 345 350  
 Leu Pro Pro Pro Asn Glu Glu Val Pro Pro Pro Leu Pro Pro Glu Glu  
 355 360 365  
 Pro Gln Ser Glu Asp Pro Glu Glu Asp Ala Arg Leu Lys Gln Leu Gln  
 370 375 380  
 Ala Ala Ala Ala His Trp Gln Gln His Gln Gln His Arg Val Gly Phe  
 385 390 395 400  
 Gln Tyr Gln Gly Ile Met Gln Lys His Thr Gln Leu Gln Gln Ile Leu  
 405 410 415  
 Gln Gln Tyr Gln Gln Ile Ile Gln Pro Pro Pro His Ile Gln Thr Met  
 420 425 430  
 Ser Val Asp Met Gln Leu Arg His Tyr Glu Met Gln Gln Gln Phe  
 435 440 445  
 Gln His Leu Tyr Gln Glu Trp Glu Arg Glu Phe Gln Leu Trp Glu Glu  
 450 455 460  
 Gln Leu His Ser Tyr Pro His Lys Asp Gln Leu Gln Glu Tyr Glu Lys  
 465 470 475 480  
 Gln Trp Lys Thr Trp Gln Gly His Met Lys Ala Thr Gln Ser Tyr Leu  
 485 490 495  
 Gln Glu Lys Val Asn Ser Phe Gln Asn Met Lys Asn Gln Tyr Met Gly  
 500 505 510  
 Asn Met Ser Met Pro Pro Pro Phe Val Pro Tyr Ser Gln Met Pro Pro  
 515 520 525  
 Pro Leu Pro Thr Met Pro Pro Pro Val Leu Pro Pro Ser Leu Pro Pro  
 530 535 540  
 Pro Val Met Pro Pro Ala Leu Pro Ala Thr Val Pro Pro Pro Gly Met  
 545 550 555 560  
 Pro Pro Pro Val Met Pro Pro Ser Leu Pro Thr Ser Val Pro Pro Pro  
 565 570 575  
 Gly Met Pro Pro Ser Leu Ser Ser Ala Gly Pro Pro Pro Val Leu Pro  
 580 585 590  
 Pro Pro Ser Leu Ser Ser Ala Gly Pro Pro Pro Val Leu Pro Pro Pro  
 595 600 605  
 Ser Leu Ser Ser Thr Ala Pro Pro Pro Val Met Pro Leu Pro Pro Leu  
 610 615 620  
 Ser Ser Ala Thr Pro Pro Pro Gly Ile Pro Pro Gly Val Pro Gln  
 625 630 635 640  
 Gly Ile Pro Pro Gln Leu Thr Ala Ala Pro Val Pro Pro Ala Ser Ser  
 645 650 655  
 Ser Gln Ser Ser Gln Val Pro Glu Lys Pro Arg Pro Ala Leu Leu Pro  
 660 665 670  
 Thr Pro Val Ser Phe Gly Ser Ala Pro Pro Thr Thr Tyr His Pro Pro  
 675 680 685  
 Leu Gln Ser Ala Gly Pro Ser Glu Gln Val Asn Ser Lys Ala Pro Leu  
 690 695 700  
 Ser Lys Ser Ala Leu Pro Tyr Ser Ser Phe Ser Ser Asp Gln Gly Leu  
 705 710 715 720

Gly	Glu	Ser	Ser	Ala	Ala	Pro	Ser	Gln	Pro	Ile	Thr	Ala	Val	Lys	Asp
				725					730					735	
Met	Pro	Val	Arg	Ser	Gly	Gly	Leu	Leu	Pro	Asp	Pro	Pro	Arg	Ser	Ser
			740					745					750		
Tyr	Leu	Glu	Ser	Pro	Arg	Gly	Pro	Arg	Phe	Asp	Gly	Pro	Arg	Arg	Phe
		755					760					765			
Glu	Asp	Leu	Gly	Ser	Arg	Cys	Glu	Gly	Pro	Arg	Pro	Lys	Gly	Pro	Arg
	770					775					780				
Phe	Glu	Gly	Asn	Arg	Pro	Asp	Gly	Pro	Arg	Pro	Arg	Tyr	Glu	Gly	His
785					790					795					800
Pro	Ala	Glu	Gly	Thr	Lys	Ser	Lys	Trp	Gly	Met	Ile	Pro	Arg	Gly	Pro
				805					810					815	
Ala	Ser	Gln	Phe	Tyr	Ile	Thr	Pro	Ser	Thr	Ser	Leu	Ser	Pro	Arg	Gln
			820					825					830		
Ser	Gly	Pro	Gln	Trp	Lys	Gly	Pro	Lys	Pro	Ala	Phe	Gly	Gln	Gln	His
		835					840					845			
Gln	Gln	Gln	Pro	Lys	Ser	Gln	Ala	Glu	Pro	Leu	Ser	Gly	Asn	Lys	Glu
	850					855					860				
Pro	Leu	Ala	Asp	Thr	Ser	Ser	Asn	Gln	Gln	Lys	Asn	Phe	Lys	Met	Gln
865					870					875					880
Ser	Ala	Ala	Phe	Ser	Ile	Ala	Ala	Asp	Val	Lys	Asp	Val	Lys	Ala	Ala
				885					890					895	
Gln	Ser	Asn	Glu	Asn	Leu	Ser	Asp	Ser	Gln	Gln	Glu	Pro	Pro	Lys	Ser
		900						905					910		
Glu	Val	Ser	Glu	Gly	Pro	Val	Glu	Pro	Ser	Asn	Trp	Asp	Gln	Asn	Val
		915					920					925			
Gln	Ser	Met	Glu	Thr	Gln	Ile	Asp	Lys	Ala	Gln	Ala	Val	Thr	Gln	Pro
	930					935					940				
Val	Pro	Leu	Ala	Asn	Lys	Pro	Val	Pro	Ala	Gln	Ser	Thr	Phe	Pro	Ser
945					950					955					960
Lys	Thr	Gly	Gly	Met	Glu	Gly	Gly	Thr	Ala	Val	Ala	Thr	Ser	Ser	Leu
				965					970					975	
Thr	Ala	Asp	Asn	Asp	Phe	Lys	Pro	Val	Gly	Ile	Gly	Leu	Pro	His	Ser
			980					985						990	
Glu	Asn	Asn	Gln	Asp	Lys	Gly	Leu	Pro	Arg	Pro	Asp	Asn	Arg	Asp	Asn
	995						1000						1005		
Arg	Leu	Glu	Gly	Asn	Arg	Gly	Asn	Ser	Ser	Ser	Tyr	Arg	Gly	Pro	
	1010					1015					1020				
Gly	Gln	Ser	Arg	Met	Glu	Asp	Thr	Arg	Asp	Lys	Gly	Leu	Val	Asn	
	1025					1030					1035				
Arg	Gly	Arg	Gly	Gln	Ala	Ile	Ser	Arg	Gly	Pro	Gly	Leu	Val	Lys	
	1040					1045					1050				
Gln	Glu	Asp	Phe	Arg	Asp	Lys	Met	Met	Gly	Arg	Arg	Glu	Asp	Ser	
	1055					1060					1065				
Arg	Glu	Lys	Met	Asn	Arg	Gly	Glu	Gly	Ser	Arg	Asp	Arg	Gly	Leu	
	1070					1075					1080				
Val	Arg	Pro	Gly	Ser	Ser	Arg	Glu	Lys	Val	Pro	Gly	Gly	Leu	Gln	
	1085					1090					1095				
Gly	Ser	Gln	Asp	Arg	Gly	Ala	Ala	Gly	Ser	Arg	Glu	Arg	Gly	Pro	
	1100					1105					1110				
Pro	Arg	Arg	Ala	Gly	Ser	Gln	Glu	Arg	Gly	Pro	Leu	Arg	Arg	Ala	
	1115					1120					1125				
Gly	Ser	Arg	Glu	Arg	Ile	Pro	Pro	Arg	Arg	Ala	Gly	Ser	Arg	Glu	
	1130					1135					1140				
Arg	Gly	Pro	Pro	Arg	Gly	Pro	Gly	Ser	Arg	Glu	Arg	Gly	Leu	Gly	
	1145					1150					1155				
Arg	Ser	Asp	Phe	Gly	Arg	Asp	Arg	Gly	Pro	Phe	Arg	Pro	Glu	Pro	
	1160					1165					1170				
Gly	Asp	Gly	Gly	Glu	Lys	Met	Tyr	Pro	Tyr	His	Arg	Asp	Glu	Pro	
	1175					1180					1185				
Pro	Arg	Ala	Pro	Trp	Asn	His	Gly	Glu	Glu	Arg	Gly	His	Glu	Glu	
	1190					1195					1200				

Phe	Pro	Leu	Asp	Gly	Arg	Asn	Ala	Pro	Met	Glu	Arg	Glu	Arg	Leu
1205						1210								
Asp	Asp	Trp	Asp	Arg	Glu	Arg	Tyr	Trp	Arg	Glu	Cys	Glu	Arg	Asp
1220						1225								
Tyr	Gln	Asp	Asp	Thr	Leu	Glu	Leu	Tyr	Asn	Arg	Glu	Asp	Arg	Phe
1235						1240								
Ser	Ala	Pro	Pro	Ser	Arg	Ser	His	Asp	Gly	Asp	Arg	Arg	Gly	Pro
1250						1255								
Trp	Trp	Asp	Asp	Trp	Glu	Arg	Asp	Gln	Asp	Met	Asp	Glu	Asp	Tyr
1265						1270								
Asn	Arg	Glu	Met	Glu	Arg	Asp	Met	Asp	Arg	Asp	Val	Asp	Arg	Ile
1280						1285								
Ser	Arg	Pro	Met	Asp	Met	Tyr	Asp	Arg	Ser	Leu	Asp	Asn	Glu	Trp
1295						1300								
Asp	Arg	Asp	Tyr	Gly	Arg	Pro	Leu	Asp	Glu	Gln	Glu	Ser	Gln	Phe
1310						1315								
Arg	Glu	Arg	Asp	Ile	Pro	Ser	Leu	Pro	Pro	Leu	Pro	Pro	Leu	Pro
1325						1330								
Pro	Leu	Pro	Pro	Leu	Asp	Arg	Tyr	Arg	Asp	Asp	Arg	Trp	Arg	Glu
1340						1345								
Glu	Arg	Asn	Arg	Glu	His	Gly	Tyr	Asp	Arg	Asp	Phe	Arg	Asp	Arg
1355						1360								
Gly	Glu	Leu	Arg	Ile	Arg	Glu	Tyr	Pro	Glu	Arg	Gly	Asp	Thr	Trp
1370						1375								
Arg	Glu	Lys	Arg	Asp	Tyr	Val	Pro	Asp	Arg	Met	Asp	Trp	Glu	Arg
1385						1390								
Glu	Arg	Leu	Ser	Asp	Arg	Trp	Tyr	Pro	Ser	Asp	Val	Asp	Arg	His
1400						1405								
Ser	Pro	Met	Ala	Glu	His	Met	Pro	Ser	Ser	His	His	Ser	Ser	Glu
1415						1420								
Met	Met	Gly	Ser	Asp	Ala	Ser	Leu	Asp	Ser	Asp	Gln	Gly	Leu	Gly
1430						1435								
Gly	Val	Met	Val	Leu	Ser	Gln	Arg	Gln	His	Glu	Ile	Ile	Leu	Lys
1445						1450								
Ala	Ala	Gln	Glu	Leu	Lys	Met	Leu	Arg	Glu	Gln	Lys	Glu	Gln	Leu
1460						1465								
Gln	Lys	Met	Lys	Asp	Phe	Gly	Ser	Glu	Pro	Gln	Met	Ala	Asp	His
1475						1480								
Leu	Pro	Pro	Gln	Glu	Ser	Arg	Leu	Gln	Asn	Thr	Ser	Ser	Arg	Pro
1490						1495								
Gly	Met	Tyr	Pro	Pro	Pro	Gly	Ser	Tyr	Arg	Pro	Pro	Pro	Pro	Met
1505						1510								
Gly	Lys	Pro	Pro	Gly	Ser	Ile	Val	Arg	Pro	Ser	Ala	Pro	Pro	Ala
1520						1525								
Arg	Ser	Ser	Val	Pro	Val	Thr	Arg	Pro	Pro	Val	Pro	Ile	Pro	Pro
1535						1540								
Pro	Pro	Pro	Pro	Pro	Pro	Leu	Pro	Pro	Pro	Pro	Pro	Val	Ile</	

Leu	Pro	Glu	Arg	Ser	Thr	Phe	Glu	Thr	Glu	His	Ala	Gly	Gln	Arg
1670						1675					1680			
Asp	Arg	Tyr	Asp	Arg	Glu	Arg	Asp	Arg	Glu	Pro	Tyr	Phe	Asp	Arg
1685						1690					1695			
Gln	Ser	Asn	Val	Ile	Ala	Asp	His	Arg	Asp	Phe	Lys	Arg	Asp	Arg
1700						1705					1710			
Glu	Thr	His	Arg	Asp	Arg	Asp	Arg	Asp	Arg	Gly	Val	Ile	Asp	Tyr
1715						1720					1725			
Asp	Arg	Asp	Arg	Phe	Asp	Arg	Glu	Arg	Arg	Pro	Arg	Asp	Asp	Arg
1730						1735					1740			
Ala	Gln	Ser	Tyr	Arg	Asp	Lys	Lys	Asp	His	Ser	Ser	Ser	Arg	Arg
1745						1750					1755			
Gly	Gly	Phe	Asp	Arg	Pro	Ser	Tyr	Asp	Arg	Lys	Ser	Asp	Arg	Pro
1760						1765					1770			
Val	Tyr	Glu	Gly	Pro	Ser	Met	Phe	Gly	Gly	Glu	Arg	Arg	Thr	Tyr
1775						1780					1785			
Pro	Glu	Glu	Arg	Met	Pro	Leu	Pro	Ala	Pro	Ser	Leu	Ser	His	Gln
1790						1795					1800			
Pro	Pro	Pro	Ala	Pro	Arg	Val	Glu	Lys	Lys	Pro	Glu	Ser	Lys	Asn
1805						1810					1815			
Val	Asp	Asp	Ile	Leu	Lys	Pro	Pro	Gly	Arg	Glu	Ser	Arg	Pro	Glu
1820						1825					1830			
Arg	Ile	Val	Val	Ile	Met	Arg	Gly	Leu	Pro	Gly	Ser	Gly	Lys	Thr
1835						1840					1845			
His	Val	Ala	Lys	Leu	Ile	Arg	Asp	Lys	Glu	Val	Glu	Phe	Gly	Gly
1850						1855					1860			
Pro	Ala	Pro	Arg	Val	Leu	Ser	Leu	Asp	Asp	Tyr	Phe	Ile	Thr	Glu
1865						1870					1875			
Val	Glu	Lys	Glu	Glu	Lys	Asp	Pro	Asp	Ser	Gly	Lys	Lys	Val	Lys
1880						1885					1890			
Lys	Lys	Val	Met	Glu	Tyr	Glu	Tyr	Glu	Ala	Glu	Met	Glu	Glu	Thr
1895						1900					1905			
Tyr	Arg	Thr	Ser	Met	Phe	Lys	Thr	Phe	Lys	Lys	Thr	Leu	Asp	Asp
1910						1915					1920			
Gly	Phe	Phe	Pro	Phe	Ile	Ile	Leu	Asp	Ala	Ile	Asn	Asp	Arg	Val
1925						1930					1935			
Arg	His	Phe	Asp	Gln	Phe	Trp	Ser	Ala	Ala	Lys	Thr	Lys	Gly	Phe
1940						1945					1950			
Glu	Val	Tyr	Leu	Ala	Glu	Met	Ser	Ala	Asp	Asn	Gln	Thr	Cys	Gly
1955						1960					1965			
Lys	Arg	Asn	Ile	His	Gly	Arg	Lys	Leu	Lys	Glu	Ile	Asn	Lys	Met
1970						1975					1980			
Ala	Asp	His	Trp	Glu	Thr	Ala	Pro	Arg	His	Met	Met	Arg	Leu	Asp
1985						1990					1995			
Ile	Arg	Ser	Leu	Leu	Gln	Asp	Ala	Ala	Ile	Glu	Glu	Val	Glu	Met
2000						2005					2010			
Glu	Asp	Phe	Asp	Ala	Asn	Ile	Glu	Glu	Gln	Lys	Glu	Glu	Lys	Lys
2015						2020					2025			
Asp	Ala	Glu	Glu	Glu	Glu	Ser	Glu	Leu	Gly	Tyr	Ile	Pro	Lys	Ser
2030						2035					2040			
Lys	Trp	Glu	Met	Asp	Thr	Ser	Glu	Ala	Lys	Leu	Asp	Lys	Leu	Asp
2045						2050					2055			
Gly	Leu	Arg	Thr	Gly	Thr	Lys	Arg	Lys	Arg	Asp	Trp	Glu	Ala	Ile
2060						2065					2070			
Ala	Ser	Arg	Met	Glu	Asp	Tyr	Leu	Gln	Leu	Pro	Asp	Asp	Tyr	Asp
2075						2080					2085			
Thr	Arg	Ala	Ser	Glu	Ala	Lys	Ala	Ser	Arg	Ser	Phe	Phe	Val	Cys
2090						2095					2100			
His	Leu	Ala	Ser	Thr	Phe	Gln	Phe	Leu	Phe	Cys	Phe	Tyr	Cys	Phe
2105						2110					2115			
Ser	Phe	Phe	Asp	Ala	Glu	Glu	Glu	Glu	Ser	Glu	Leu	Val	Gly	Asp
2120						2125					2130			

Arg Pro Thr Thr Leu Asn Ser Val Ser Leu Leu Lys Phe Leu Lys  
 2135 2140 2145  
 Lys Val 2150

<210> 281

<211> 979

<212> PRT

<213> Homo sapiens

<400> 281

Met Ser Val Leu Gly Glu Tyr Glu Arg His Cys Asp Ser Ile Asn Ser  
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 35 40 45  
 Glu Leu His Tyr Ile Pro Ile Arg Val Leu Gly Arg Gly Ala Phe Gly  
 50 55 60  
 Glu Ala Thr Leu Tyr Arg Arg Thr Glu Asp Asp Ser Leu Val Val Trp  
 65 70 75 80  
 Lys Glu Val Asp Leu Thr Arg Leu Ser Glu Lys Glu Arg Arg Asp Ala  
 85 90 95  
 Leu Asn Glu Ile Val Ile Leu Ala Leu Leu Gln His Asp Asn Ile Ile  
 100 105 110  
 Ala Tyr Tyr Asn His Phe Met Asp Asn Thr Thr Leu Leu Ile Glu Leu  
 115 120 125  
 Glu Tyr Cys Asn Gly Gly Asn Leu Tyr Asp Lys Ile Leu Arg Gln Lys  
 130 135 140  
 Asp Lys Leu Phe Glu Glu Glu Met Val Val Trp Tyr Leu Phe Gln Ile  
 145 150 155 160  
 Val Ser Ala Val Ser Cys Ile His Lys Ala Gly Ile Leu His Arg Asp  
 165 170 175  
 Ile Lys Thr Leu Asn Ile Phe Leu Thr Lys Ala Asn Leu Ile Lys Leu  
 180 185 190  
 Gly Asp Tyr Gly Leu Ala Lys Lys Leu Asn Ser Glu Tyr Ser Met Ala  
 195 200 205  
 Glu Thr Leu Val Gly Thr Pro Tyr Tyr Met Ser Pro Glu Leu Cys Gln  
 210 215 220  
 Gly Val Lys Tyr Asn Phe Lys Ser Asp Ile Trp Ala Val Gly Cys Val  
 225 230 235 240  
 Ile Phe Glu Leu Leu Thr Leu Lys Arg Thr Phe Asp Ala Thr Asn Pro  
 245 250 255  
 Leu Asn Leu Cys Val Lys Ile Val Gln Gly Ile Arg Ala Met Glu Val  
 260 265 270  
 Asp Ser Ser Gln Tyr Ser Leu Glu Leu Ile Gln Met Val His Ser Cys  
 275 280 285  
 Leu Asp Gln Asp Pro Glu Gln Arg Pro Thr Ala Asp Glu Leu Leu Asp  
 290 295 300  
 Arg Pro Leu Leu Arg Lys Arg Arg Arg Glu Met Glu Glu Lys Val Thr  
 305 310 315 320  
 Leu Leu Asn Ala Pro Thr Lys Arg Pro Arg Ser Ser Thr Val Thr Glu  
 325 330 335  
 Ala Pro Ile Ala Val Val Thr Ser Arg Thr Ser Glu Val Tyr Ile Trp  
 340 345 350  
 Gly Gly Gly Lys Ser Thr Pro Gln Lys Leu Asp Val Ile Lys Ser Gly  
 355 360 365

Cys	Ser	Ala	Arg	Gln	Val	Cys	Ala	Gly	Asn	Thr	His	Phe	Ala	Val	Val
370						375					380				
Thr	Val	Glu	Lys	Glu	Leu	Tyr	Thr	Trp	Val	Asn	Met	Gln	Gly	Gly	Thr
385					390					395					400
Lys	Leu	His	Gly	Gln	Leu	Gly	His	Gly	Asp	Lys	Ala	Ser	Tyr	Arg	Gln
				405					410					415	
Pro	Lys	His	Val	Glu	Lys	Leu	Gln	Gly	Lys	Ala	Ile	His	Gln	Val	Ser
			420					425					430		
Cys	Gly	Asp	Asp	Phe	Thr	Val	Cys	Val	Thr	Asp	Glu	Gly	Gln	Leu	Tyr
		435					440					445			
Ala	Phe	Gly	Ser	Asp	Tyr	Tyr	Gly	Cys	Met	Gly	Val	Asp	Lys	Val	Ala
	450					455					460				
Gly	Pro	Glu	Val	Leu	Glu	Pro	Met	Gln	Leu	Asn	Phe	Phe	Leu	Ser	Asn
465					470					475					480
Pro	Val	Glu	Gln	Val	Ser	Cys	Gly	Asp	Asn	His	Val	Val	Val	Leu	Thr
				485					490					495	
Arg	Asn	Lys	Glu	Val	Tyr	Ser	Trp	Gly	Cys	Gly	Glu	Tyr	Gly	Arg	Leu
			500					505					510		
Gly	Leu	Asp	Ser	Glu	Glu	Asp	Tyr	Tyr	Thr	Pro	Gln	Lys	Val	Asp	Val
		515					520					525			
Pro	Lys	Ala	Leu	Ile	Ile	Val	Ala	Val	Gln	Cys	Gly	Cys	Asp	Gly	Thr
	530					535					540				
Phe	Leu	Leu	Thr	Gln	Ser	Gly	Lys	Val	Leu	Ala	Cys	Gly	Leu	Asn	Glu
545					550					555					560
Phe	Asn	Lys	Leu	Gly	Leu	Asn	Gln	Cys	Met	Ser	Gly	Ile	Ile	Asn	His
				565					570					575	
Glu	Ala	Tyr	His	Glu	Val	Pro	Tyr	Thr	Thr	Ser	Phe	Thr	Leu	Ala	Lys
			580					585					590		
Gln	Leu	Ser	Phe	Tyr	Lys	Ile	Arg	Thr	Ile	Ala	Pro	Gly	Lys	Thr	His
		595					600					605			
Thr	Ala	Ala	Ile	Asp	Glu	Arg	Gly	Arg	Leu	Leu	Thr	Phe	Gly	Cys	Asn
	610					615					620				
Lys	Cys	Gly	Gln	Leu	Gly	Val	Gly	Asn	Tyr	Lys	Lys	Arg	Leu	Gly	Ile
625					630					635					640
Asn	Leu	Leu	Gly	Gly	Pro	Leu	Gly	Gly	Lys	Gln	Val	Ile	Arg	Val	Ser
			645						650					655	
Cys	Gly	Asp	Glu	Phe	Thr	Ile	Ala	Ala	Thr	Asp	Asp	Asn	His	Ile	Phe
			660					665					670		
Ala	Trp	Gly	Asn	Gly	Gly	Asn	Gly	Arg	Leu	Ala	Met	Thr	Pro	Thr	Glu
		675					680						685		
Arg	Pro	His	Gly	Ser	Asp	Ile	Cys	Thr	Ser	Trp	Pro	Arg	Pro	Ile	Phe
	690					695					700				
Gly	Ser	Leu	His	His	Val	Pro	Asp	Leu	Ser	Cys	Arg	Gly	Trp	His	Thr
705					710					715					720
Ile	Leu	Ile	Val	Glu	Lys	Val	Leu	Asn	Ser	Lys	Thr	Ile	Arg	Ser	Asn
				725					730					735	
Ser	Ser	Gly	Leu	Ser	Ile	Gly	Thr	Val	Phe	Gln	Ser	Ser	Ser	Pro	Gly
			740					745					750		
Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Glu	Glu	Glu	Asp	Ser	Gln	Gln	Glu
		755					760					765			
Ser	Glu	Thr	Pro	Asp	Pro	Ser	Gly	Gly	Phe	Arg	Gly	Thr	Met	Glu	Ala
	770					775					780				
Asp	Arg	Gly	Met	Glu	Gly	Leu	Ile	Ser	Pro	Thr	Glu	Ala	Met	Gly	Asn
785					790					795					800
Ser	Asn	Gly	Ala	Ser	Ser	Ser	Cys	Pro	Gly	Trp	Leu	Arg	Lys	Glu	Leu
				805					810					815	
Glu	Asn	Ala	Glu	Phe	Ile	Pro	Met	Pro	Asp	Ser	Pro	Ser	Pro	Leu	Ser
		820						825					830		
Ala	Ala	Phe	Ser	Glu	Ser	Glu	Lys	Asp	Thr	Leu	Pro	Tyr	Glu	Glu	Leu
		835					840					845			
Gln	Gly	Leu	Lys	Val	Ala	Ser	Glu	Ala	Pro	Leu	Glu	His	Lys	Pro	Gln
	850					855					860				

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Val Glu Ala Ser Ser Pro Arg Leu Asn Pro Ala Val Thr Cys Ala Gly  
 865 870 875 880  
 Lys Gly Thr Pro Leu Thr Pro Pro Ala Cys Ala Cys Ser Ser Leu Gln  
 885 890 895  
 Val Glu Val Glu Arg Leu Gln Gly Leu Val Leu Lys Cys Leu Ala Glu  
 900 905 910  
 Gln Gln Lys Leu Gln Gln Glu Asn Leu Gln Ile Phe Thr Gln Leu Gln  
 915 920 925  
 Lys Leu Asn Lys Lys Leu Glu Gly Gly Gln Gln Val Gly Met His Ser  
 930 935 940  
 Lys Gly Thr Gln Thr Ala Lys Glu Glu Met Glu Met Asp Pro Lys Pro  
 945 950 955 960  
 Asp Leu Asp Ser Asp Ser Gly Cys Leu Leu Gly Thr Asp Ser Cys Arg  
 965 970 975  
 Pro Ser Leu

&lt;210&gt; 282

&lt;211&gt; 107

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 282

Met Arg Phe Phe Leu Phe Phe Phe Phe Phe Leu Arg Trp Ser Leu Val  
 1 5 10 15  
 Ser Pro Arg Leu Glu Cys Ser Gly Leu Val Leu Ala His Cys Asn Leu  
 20 25 30  
 His Leu Leu Gly Ser Arg Glu Ser Pro Ala Ser Ala Ser Arg Val Ala  
 35 40 45  
 Gly Ile Thr Gly Val Ser His His Thr Gln Thr His Leu Met Ser Phe  
 50 55 60  
 Asp Val Lys Ala Cys Asn Ser Asn Pro Tyr Val Trp Asn Ile Cys Ile  
 65 70 75 80  
 Thr Ser Glu Phe Phe His Leu Val Asn Ser Cys Thr Ser Leu Ser Cys  
 85 90 95  
 Pro Phe Phe Pro Pro Leu Ala Val Ser Tyr Cys  
 100 105

&lt;210&gt; 283

&lt;211&gt; 533

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 283

Met Thr Lys Lys Arg Ile Ala Val Ile Gly Gly Gly Val Ser Gly Leu  
 1 5 10 15  
 Ser Ser Ile Lys Cys Cys Val Glu Glu Gly Leu Glu Pro Val Cys Phe  
 20 25 30  
 Glu Arg Thr Asp Asp Ile Gly Gly Leu Trp Arg Phe Gln Glu Asn Pro  
 35 40 45  
 Glu Glu Gly Arg Ala Ser Ile Tyr Lys Ser Val Ile Ile Asn Thr Ser  
 50 55 60

Lys Glu Met Met Cys Phe Ser Asp Tyr Pro Ile Pro Asp His Tyr Pro  
 65 70 75 80  
 Asn Phe Met His Asn Ala Gln Val Leu Glu Tyr Phe Arg Met Tyr Ala  
 85 90 95  
 Lys Glu Phe Asp Leu Leu Lys Tyr Ile Arg Phe Lys Thr Thr Val Cys  
 100 105 110  
 Ser Val Lys Lys Gln Pro Asp Phe Ala Thr Ser Gly Gln Trp Glu Val  
 115 120 125  
 Val Thr Glu Ser Glu Gly Lys Lys Glu Met Asn Val Phe Asp Gly Val  
 130 135 140  
 Met Val Cys Thr Gly His His Thr Asn Ala His Leu Pro Leu Glu Ser  
 145 150 155 160  
 Phe Pro Gly Ile Glu Lys Phe Lys Gly Gln Tyr Phe His Ser Arg Asp  
 165 170 175  
 Tyr Lys Asn Pro Glu Gly Phe Thr Gly Lys Arg Val Ile Ile Ile Gly  
 180 185 190  
 Ile Gly Asn Ser Gly Gly Asp Leu Ala Val Glu Ile Ser Gln Thr Ala  
 195 200 205  
 Lys Gln Val Phe Leu Ser Thr Arg Arg Gly Ala Trp Ile Leu Asn Arg  
 210 215 220  
 Val Gly Asp Tyr Gly Tyr Pro Ala Asp Val Leu Phe Ser Ser Arg Leu  
 225 230 235 240  
 Thr His Phe Ile Trp Lys Ile Cys Gly Gln Ser Leu Ala Asn Lys Tyr  
 245 250 255  
 Leu Glu Lys Lys Ile Asn Gln Arg Phe Asp His Glu Met Phe Gly Leu  
 260 265 270  
 Lys Pro Lys His Arg Ala Leu Ser Gly Leu Val Lys Val Lys Gly Asn Asp  
 275 280 285  
 Leu Pro Asn Arg Ile Ile Ser Gly Leu Val Lys Val Lys Gly Asn Val  
 290 295 300  
 Lys Glu Phe Thr Glu Thr Ala Ala Ile Phe Glu Asp Gly Ser Arg Glu  
 305 310 315 320  
 Asp Asp Ile Asp Ala Val Ile Phe Ala Thr Gly Tyr Ser Phe Asp Phe  
 325 330 335  
 Pro Phe Leu Glu Asp Ser Val Lys Val Val Lys Asn Lys Ile Pro Leu  
 340 345 350  
 Tyr Lys Lys Val Phe Pro Pro Asn Leu Glu Arg Pro Thr Leu Ala Ile  
 355 360 365  
 Ile Gly Leu Ile Gln Pro Leu Gly Ala Ile Met Pro Ile Ser Glu Leu  
 370 375 380  
 Gln Gly Arg Trp Ala Thr Gln Val Phe Lys Gly Leu Lys Thr Leu Pro  
 385 390 395 400  
 Ser Gln Ser Glu Met Met Ala Glu Ile Ser Lys Ala Gln Glu Glu Ile  
 405 410 415  
 Asp Lys Arg Tyr Val Glu Ser Gln Arg His Thr Ile Gln Gly Asp Tyr  
 420 425 430  
 Ile Asp Thr Met Glu Glu Leu Ala Asp Leu Val Gly Val Arg Pro Asn  
 435 440 445  
 Leu Leu Ser Leu Ala Phe Thr Asp Pro Lys Leu Ala Leu His Leu Leu  
 450 455 460  
 Leu Gly Pro Cys Thr Pro Ile His Tyr Arg Val Gln Gly Pro Gly Lys  
 465 470 475 480  
 Trp Asp Gly Ala Arg Lys Ala Ile Leu Thr Thr Asp Asp Arg Ile Arg  
 485 490 495  
 Lys Pro Leu Met Thr Arg Val Val Glu Arg Ser Ser Ser Met Thr Ser  
 500 505 510  
 Thr Met Thr Ile Gly Lys Phe Met Leu Ala Leu Ala Phe Phe Ala Ile  
 515 520 525  
 Ile Ile Ala Tyr Phe  
 530



&lt;210&gt; 284

&lt;211&gt; 757

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 284

Met Val Pro Asp Thr Ala Cys Val Leu Leu Leu Thr Leu Ala Ala Leu  
 1 5 10 15  
 Gly Ala Ser Gly Gln Gly Gln Ser Pro Leu Gly Ser Asp Leu Gly Pro  
 20 25 30  
 Gln Met Leu Arg Glu Leu Gln Glu Thr Asn Ala Ala Leu Gln Asp Val  
 35 40 45  
 Arg Asp Trp Leu Arg Gln Gln Val Arg Glu Ile Thr Phe Leu Lys Asn  
 50 55 60  
 Thr Val Met Glu Cys Asp Ala Cys Gly Met Gln Gln Ser Val Arg Thr  
 65 70 75 80  
 Gly Leu Pro Ser Val Arg Pro Leu Leu His Cys Ala Pro Gly Phe Cys  
 85 90 95  
 Phe Pro Gly Val Ala Cys Ile Gln Thr Glu Ser Gly Gly Arg Cys Gly  
 100 105 110  
 Pro Cys Pro Ala Gly Phe Thr Gly Asn Gly Ser His Cys Thr Asp Val  
 115 120 125  
 Asn Glu Cys Asn Ala His Pro Cys Phe Pro Arg Val Arg Cys Ile Asn  
 130 135 140  
 Thr Ser Pro Gly Phe Arg Cys Glu Ala Cys Pro Pro Gly Tyr Ser Gly  
 145 150 155 160  
 Pro Thr His Gln Gly Val Gly Leu Ala Phe Ala Lys Ala Asn Lys Gln  
 165 170 175  
 Val Cys Thr Asp Ile Asn Glu Cys Glu Thr Gly Gln His Asn Cys Val  
 180 185 190  
 Pro Asn Ser Val Cys Ile Asn Thr Arg Gly Ser Phe Gln Cys Gly Pro  
 195 200 205  
 Cys Gln Pro Gly Phe Val Gly Asp Gln Ala Ser Gly Cys Gln Arg Gly  
 210 215 220  
 Ala Gln Arg Phe Cys Pro Asp Gly Ser Pro Ser Glu Cys His Glu His  
 225 230 235 240  
 Ala Asp Cys Val Leu Glu Arg Asp Gly Ser Arg Ser Cys Val Cys Arg  
 245 250 255  
 Val Gly Trp Ala Gly Asn Gly Ile Leu Cys Gly Arg Asp Thr Asp Leu  
 260 265 270  
 Asp Gly Phe Pro Asp Glu Lys Leu Arg Cys Pro Glu Pro Gln Cys Arg  
 275 280 285  
 Lys Asp Asn Cys Val Thr Val Pro Asn Ser Gly Gln Glu Asp Val Asp  
 290 295 300  
 Arg Asp Gly Ile Gly Asp Ala Cys Asp Pro Asp Ala Asp Gly Asp Gly  
 305 310 315 320  
 Val Pro Asn Glu Lys Asp Asn Cys Pro Leu Val Arg Asn Pro Asp Gln  
 325 330 335  
 Arg Asn Thr Asp Glu Asp Lys Trp Gly Asp Ala Cys Asp Asn Cys Arg  
 340 345 350  
 Ser Gln Lys Asn Asp Asp Gln Lys Asp Thr Asp Gln Asp Gly Arg Gly  
 355 360 365  
 Asp Ala Cys Asp Asp Asp Ile Asp Gly Asp Arg Ile Arg Asn Gln Ala  
 370 375 380  
 Asp Asn Cys Pro Arg Val Pro Asn Ser Asp Gln Lys Asp Ser Asp Gly  
 385 390 395 400

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Asp Gly Ile Gly Asp Ala Cys Asp Asn Cys Pro Gln Lys Ser Asn Pro  
 405 410 415  
 Asp Gln Ala Asp Val Asp His Asp Phe Val Gly Asp Ala Cys Asp Ser  
 420 425 430  
 Asp Gln Asp Gln Asp Gly Asp Gly His Gln Asp Ser Arg Asp Asn Cys  
 435 440 445  
 Pro Thr Val Pro Asn Ser Ala Gln Glu Asp Ser Asp His Asp Gly Gln  
 450 455 460  
 Gly Asp Ala Cys Asp Asp Asp Asp Asn Asp Gly Val Pro Asp Ser  
 465 470 475 480  
 Arg Asp Asn Cys Arg Leu Val Pro Asn Pro Gly Gln Glu Asp Ala Asp  
 485 490 495  
 Arg Asp Gly Val Gly Asp Val Cys Gln Asp Asp Phe Asp Ala Asp Lys  
 500 505 510  
 Val Val Asp Lys Ile Asp Val Cys Pro Glu Asn Ala Glu Val Thr Leu  
 515 520 525  
 Thr Asp Phe Arg Ala Phe Gln Thr Val Val Leu Asp Pro Glu Gly Asp  
 530 535 540  
 Ala Gln Ile Asp Pro Asn Trp Val Val Leu Asn Gln Gly Arg Glu Ile  
 545 550 555 560  
 Val Gln Thr Met Asn Ser Asp Pro Gly Leu Ala Val Gly Tyr Thr Ala  
 565 570 575  
 Phe Asn Gly Val Asp Phe Glu Gly Thr Phe His Val Asn Thr Val Thr  
 580 585 590  
 Asp Asp Asp Tyr Ala Gly Phe Ile Phe Gly Tyr Gln Asp Ser Ser Ser  
 595 600 605  
 Phe Tyr Val Val Met Trp Lys Gln Met Glu Gln Thr Tyr Trp Gln Ala  
 610 615 620  
 Asn Pro Phe Arg Ala Val Ala Glu Pro Gly Ile Gln Leu Lys Ala Val  
 625 630 635 640  
 Lys Ser Ser Thr Gly Pro Gly Glu Gln Leu Arg Asn Ala Leu Trp His  
 645 650 655  
 Thr Gly Asp Thr Glu Ser Gln Val Arg Leu Leu Trp Lys Asp Pro Arg  
 660 665 670  
 Asn Val Gly Trp Lys Asp Lys Lys Ser Tyr Arg Trp Phe Leu Gln His  
 675 680 685  
 Arg Pro Gln Val Gly Tyr Ile Arg Val Arg Phe Tyr Glu Gly Pro Glu  
 690 695 700  
 Leu Val Ala Asp Ser Asn Val Val Leu Asp Thr Thr Met Arg Gly Gly  
 705 710 715 720  
 Arg Leu Gly Val Phe Cys Phe Ser Gln Glu Asn Ile Ile Trp Ala Asn  
 725 730 735  
 Leu Arg Tyr Arg Cys Asn Asp Thr Ile Pro Glu Asp Tyr Glu Thr His  
 740 745 750  
 Gln Leu Arg Gln Ala  
 755

&lt;210&gt; 285

&lt;211&gt; 3396

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 285

Met Phe Ile Asn Ile Lys Ser Ile Leu Trp Met Cys Ser Thr Leu Ile  
 1 5 10 15  
 Val Thr His Ala Leu His Lys Val Lys Val Gly Lys Ser Pro Pro Val  
 20 25 30

Arg Gly Ser Leu Ser Gly Lys Val Ser Leu Pro Cys His Phe Ser Thr  
 35 40 45  
 Met Pro Thr Leu Pro Pro Ser Tyr Asn Thr Ser Glu Phe Leu Arg Ile  
 50 55 60  
 Lys Trp Ser Lys Ile Glu Val Asp Lys Asn Gly Lys Asp Leu Lys Glu  
 65 70 75 80  
 Thr Thr Val Leu Val Ala Gln Asn Gly Asn Ile Lys Ile Gly Gln Asp  
 85 90 95  
 Tyr Lys Gly Arg Val Ser Val Pro Thr His Pro Glu Ala Val Gly Asp  
 100 105 110  
 Ala Ser Leu Thr Val Val Lys Leu Leu Ala Ser Asp Ala Gly Leu Tyr  
 115 120 125  
 Arg Cys Asp Val Met Tyr Gly Ile Glu Asp Thr Gln Asp Thr Val Ser  
 130 135 140  
 Leu Thr Val Asp Gly Val Phe His Tyr Arg Ala Ala Thr Ser Arg  
 145 150 155 160  
 Tyr Thr Leu Asn Phe Glu Ala Ala Gln Lys Ala Cys Leu Asp Val Gly  
 165 170 175  
 Ala Val Ile Ala Thr Pro Glu Gln Leu Phe Ala Ala Tyr Glu Asp Gly  
 180 185 190  
 Phe Glu Gln Cys Asp Ala Gly Trp Leu Ala Asp Gln Thr Val Arg Tyr  
 195 200 205  
 Pro Ile Arg Ala Pro Arg Val Gly Cys Tyr Gly Asp Lys Met Gly Lys  
 210 215 220  
 Ala Gly Val Arg Thr Tyr Gly Phe Arg Ser Pro Gln Glu Thr Tyr Asp  
 225 230 235 240  
 Val Tyr Cys Tyr Val Asp His Leu Asp Gly Asp Val Phe His Leu Thr  
 245 250 255  
 Val Pro Ser Lys Phe Thr Phe Glu Glu Ala Ala Lys Glu Cys Glu Asn  
 260 265 270  
 Gln Asp Ala Arg Leu Ala Thr Val Gly Glu Leu Gln Ala Ala Trp Arg  
 275 280 285  
 Asn Gly Phe Asp Gln Cys Asp Tyr Gly Trp Leu Ser Asp Ala Ser Val  
 290 295 300  
 Arg His Pro Val Thr Val Ala Arg Ala Gln Cys Gly Gly Leu Leu  
 305 310 315 320  
 Gly Val Arg Thr Leu Tyr Arg Phe Glu Asn Gln Thr Gly Phe Pro Pro  
 325 330 335  
 Pro Asp Ser Arg Phe Asp Ala Tyr Cys Phe Lys Pro Lys Glu Ala Thr  
 340 345 350  
 Thr Ile Asp Leu Ser Ile Leu Ala Glu Thr Ala Ser Pro Ser Leu Ser  
 355 360 365  
 Lys Glu Pro Gln Met Val Ser Asp Arg Thr Thr Pro Ile Ile Pro Leu  
 370 375 380  
 Val Asp Glu Leu Pro Val Ile Pro Thr Glu Phe Pro Pro Val Gly Asn  
 385 390 395 400  
 Ile Val Ser Phe Glu Gln Lys Ala Thr Val Gln Pro Gln Ala Ile Thr  
 405 410 415  
 Asp Ser Leu Ala Thr Lys Leu Pro Thr Pro Thr Gly Ser Thr Lys Lys  
 420 425 430  
 Pro Trp Asp Met Asp Asp Tyr Ser Pro Ser Ala Ser Gly Pro Leu Gly  
 435 440 445  
 Lys Leu Asp Ile Ser Glu Ile Lys Glu Glu Val Leu Gln Ser Thr Thr  
 450 455 460  
 Gly Val Ser His Tyr Ala Thr Asp Ser Trp Asp Gly Val Val Glu Asp  
 465 470 475 480  
 Lys Gln Thr Gln Glu Ser Val Thr Gln Ile Glu Gln Ile Glu Val Gly  
 485 490 495  
 Pro Leu Val Thr Ser Met Glu Ile Leu Lys His Ile Pro Ser Lys Glu  
 500 505 510  
 Phe Pro Val Thr Glu Thr Pro Leu Val Thr Ala Arg Met Ile Leu Glu  
 515 520 525

Ser	Lys	Thr	Glu	Lys	Lys	Met	Val	Ser	Thr	Val	Ser	Glu	Leu	Val	Thr
	530					535					540				
Thr	Gly	His	Tyr	Gly	Phe	Thr	Leu	Gly	Glu	Glu	Asp	Asp	Glu	Asp	Arg
545					550					555					560
Thr	Leu	Thr	Val	Gly	Ser	Asp	Glu	Ser	Thr	Leu	Ile	Phe	Asp	Gln	Ile
				565					570					575	
Pro	Glu	Val	Ile	Thr	Val	Ser	Lys	Thr	Ser	Glu	Asp	Thr	Ile	His	Thr
			580					585					590		
His	Leu	Glu	Asp	Leu	Glu	Ser	Val	Ser	Ala	Ser	Thr	Thr	Val	Ser	Pro
		595					600					605			
Leu	Ile	Met	Pro	Asp	Asn	Asn	Gly	Ser	Ser	Met	Asp	Asp	Trp	Glu	Glu
	610				615						620				
Arg	Gln	Thr	Ser	Gly	Arg	Ile	Thr	Glu	Glu	Phe	Leu	Gly	Lys	Tyr	Leu
625					630					635					640
Ser	Thr	Thr	Pro	Phe	Pro	Ser	Gln	His	Arg	Thr	Glu	Ile	Glu	Leu	Phe
				645					650					655	
Pro	Tyr	Ser	Gly	Asp	Lys	Ile	Leu	Val	Glu	Gly	Ile	Ser	Thr	Val	Ile
			660					665						670	
Tyr	Pro	Ser	Leu	Gln	Thr	Glu	Met	Thr	His	Arg	Arg	Glu	Arg	Thr	Glu
		675					680					685			
Thr	Leu	Ile	Pro	Glu	Met	Arg	Thr	Asp	Thr	Tyr	Thr	Asp	Glu	Ile	Gln
	690					695						700			
Glu	Glu	Ile	Thr	Lys	Ser	Pro	Phe	Met	Gly	Lys	Thr	Glu	Glu	Glu	Val
705					710					715					720
Phe	Ser	Gly	Met	Lys	Leu	Ser	Thr	Ser	Leu	Ser	Glu	Pro	Ile	His	Val
				725					730					735	
Thr	Glu	Ser	Ser	Val	Glu	Met	Thr	Lys	Ser	Phe	Asp	Phe	Pro	Thr	Leu
			740					745					750		
Ile	Thr	Lys	Leu	Ser	Ala	Glu	Pro	Thr	Glu	Val	Arg	Asp	Met	Glu	Glu
		755					760					765			
Asp	Phe	Thr	Ala	Thr	Pro	Gly	Thr	Thr	Lys	Tyr	Asp	Glu	Asn	Ile	Thr
	770					775					780				
Thr	Val	Leu	Leu	Ala	His	Gly	Thr	Leu	Ser	Val	Glu	Ala	Ala	Thr	Val
785					790					795					800
Ser	Lys	Trp	Ser	Trp	Asp	Glu	Asp	Asn	Thr	Thr	Ser	Lys	Pro	Leu	Glu
			805					810						815	
Ser	Thr	Glu	Pro	Ser	Ala	Ser	Ser	Lys	Leu	Pro	Pro	Ala	Leu	Leu	Thr
			820					825					830		
Thr	Val	Gly	Met	Asn	Gly	Lys	Asp	Lys	Asp	Ile	Pro	Ser	Phe	Thr	Glu
		835					840					845			
Asp	Gly	Ala	Asp	Glu	Phe	Thr	Leu	Ile	Pro	Asp	Ser	Thr	Gln	Lys	Gln
	850					855					860				
Leu	Glu	Glu	Val	Thr	Asp	Glu	Asp	Ile	Ala	Ala	His	Gly	Lys	Phe	Thr
865					870					875					880
Ile	Arg	Phe	Gln	Pro	Thr	Thr	Ser	Thr	Gly	Ile	Ala	Glu	Lys	Ser	Thr
				885					890					895	
Leu	Arg	Asp	Ser	Thr	Thr	Glu	Glu	Lys	Val	Pro	Pro	Ile	Thr	Ser	Thr
			900					905					910		
Glu	Gly	Gln	Val	Tyr	Ala	Thr	Met	Glu	Gly	Ser	Ala	Leu	Gly	Glu	Val
		915					920					925			
Glu	Asp	Val	Asp	Leu	Ser	Lys	Pro	Val	Ser	Thr	Val	Pro	Gln	Phe	Ala
	930					935					940				
His	Thr	Ser	Glu	Val	Glu	Gly	Leu	Ala	Phe	Val	Ser	Tyr	Ser	Ser	Thr
945					950					955					960
Gln	Glu	Pro	Thr	Thr	Tyr	Val	Asp	Ser	Ser	His	Thr	Ile	Pro	Leu	Ser
				965					970					975	
Val	Ile	Pro	Lys	Thr	Asp	Trp	Gly	Val	Leu	Val	Pro	Ser	Val	Pro	Ser
			980					985					990		
Glu	Asp	Glu	Val	Leu	Gly	Glu	Pro	Ser	Gln	Asp	Ile	Leu	Val	Ile	Asp
	995						1000					1005			
Gln	Thr	Arg	Leu	Glu	Ala	Thr	Ile	Ser	Pro	Glu	Thr	Met	Arg	Thr	
1010						1015						1020			

Thr	Lys	Ile	Thr	Glu	Gly	Thr	Thr	Gln	Glu	Glu	Phe	Pro	Trp	Lys
1025						1030					1035			
Glu	Gln	Thr	Ala	Glu	Lys	Pro	Val	Pro	Ala	Leu	Ser	Ser	Thr	Ala
1040						1045					1050			
Trp	Thr	Pro	Lys	Glu	Ala	Val	Thr	Pro	Leu	Asp	Glu	Gln	Glu	Gly
1055						1060					1065			
Asp	Gly	Ser	Ala	Tyr	Thr	Val	Ser	Glu	Asp	Glu	Leu	Leu	Thr	Gly
1070						1075					1080			
Ser	Glu	Arg	Val	Pro	Val	Leu	Glu	Thr	Thr	Pro	Val	Gly	Lys	Ile
1085						1090					1095			
Asp	His	Ser	Val	Ser	Tyr	Pro	Pro	Gly	Ala	Val	Thr	Glu	His	Lys
1100						1105					1110			
Val	Lys	Thr	Asp	Glu	Val	Val	Thr	Leu	Thr	Pro	Arg	Ile	Gly	Pro
1115						1120					1125			
Lys	Val	Ser	Leu	Ser	Pro	Gly	Pro	Glu	Gln	Lys	Tyr	Glu	Thr	Glu
1130						1135					1140			
Gly	Ser	Ser	Thr	Thr	Gly	Phe	Thr	Ser	Ser	Leu	Ser	Pro	Phe	Ser
1145						1150					1155			
Thr	His	Ile	Thr	Gln	Leu	Met	Glu	Glu	Thr	Thr	Thr	Glu	Lys	Thr
1160						1165					1170			
Ser	Leu	Glu	Asp	Ile	Asp	Leu	Gly	Ser	Gly	Leu	Phe	Glu	Lys	Pro
1175						1180					1185			
Lys	Ala	Thr	Glu	Leu	Ile	Glu	Phe	Ser	Thr	Ile	Lys	Val	Thr	Val
1190						1195					1200			
Pro	Ser	Asp	Ile	Thr	Thr	Ala	Phe	Ser	Ser	Val	Asp	Arg	Leu	His
1205						1210					1215			
Thr	Thr	Ser	Ala	Phe	Lys	Pro	Ser	Ser	Ala	Ile	Thr	Lys	Lys	Pro
1220						1225					1230			
Pro	Leu	Ile	Asp	Arg	Glu	Pro	Gly	Glu	Glu	Thr	Thr	Ser	Asp	Met
1235						1240					1245			
Val	Ile	Ile	Gly	Glu	Ser	Thr	Ser	His	Val	Pro	Pro	Thr	Thr	Leu
1250						1255					1260			
Glu	Asp	Ile	Val	Ala	Lys	Glu	Thr	Glu	Thr	Asp	Ile	Asp	Arg	Glu
1265						1270					1275			
Tyr	Phe	Thr	Thr	Ser	Ser	Pro	Pro	Ala	Thr	Gln	Pro	Thr	Arg	Pro
1280						1285					1290			
Pro	Thr	Val	Glu	Asp	Lys	Glu	Ala	Phe	Gly	Pro	Gln	Ala	Leu	Ser
1295						1300					1305			
Thr	Pro	Gln	Pro	Pro	Ala	Ser	Thr	Lys	Phe	His	Pro	Asp	Ile	Asn
1310						1315					1320			
Val	Tyr	Ile	Ile	Glu	Val	Arg	Glu	Asn	Lys	Thr	Gly	Arg	Met	Ser
1325						1330					1335			
Asp	Leu	Ser	Val	Ile	Gly	His	Pro	Ile	Asp	Ser	Glu	Ser	Lys	Glu
1340						1345					1350			
Asp	Glu	Pro	Cys	Ser	Glu	Glu	Thr	Asp	Pro	Val	His	Asp	Leu	Met
1355						1360					1365			
Ala	Glu	Ile	Leu	Pro	Glu	Phe	Pro	Asp	Ile	Ile	Glu	Ile	Asp	Leu
1370						1375					1380			
Tyr	His	Ser	Glu	Glu	Asn	Glu	Glu	Glu	Glu	Glu	Glu	Cys	Ala	Asn
1385						1390					1395			
Ala	Thr	Asp	Val	Thr	Thr	Thr	Pro	Ser	Val	Gln	Tyr	Ile	Asn	Gly
1400						1405					1410			
Lys	His	Leu	Val	Thr	Thr	Val	Pro	Lys	Asp	Pro	Glu	Ala	Ala	Glu
1415						1420					1425			
Ala	Arg	Arg	Gly	Gln	Phe	Glu	Ser	Val	Ala	Pro	Ser	Gln	Asn	Phe
1430						1435					1440			
Ser	Asp	Ser	Ser	Glu	Ser	Asp	Thr	His	Pro	Phe	Val	Ile	Ala	Lys
1445						1450					1455			
Thr	Glu	Leu	Ser	Thr	Ala	Val	Gln	Pro	Asn	Glu	Ser	Thr	Glu	Thr
1460						1465					1470			
Thr	Glu	Ser	Leu	Glu	Val	Thr	Trp	Lys	Pro	Glu	Thr	Tyr	Pro	Glu
1475						1480					1485			

Thr	Ser	Glu	His	Phe	Ser	Gly	Gly	Glu	Pro	Asp	Val	Phe	Pro	Thr
1490						1495					1500			
Val	Pro	Phe	His	Glu	Glu	Phe	Glu	Ser	Gly	Thr	Ala	Lys	Lys	Gly
1505						1510					1515			
Ala	Glu	Ser	Val	Thr	Glu	Arg	Asp	Thr	Glu	Val	Gly	His	Gln	Ala
1520						1525					1530			
His	Glu	His	Thr	Glu	Pro	Val	Ser	Leu	Phe	Pro	Glu	Glu	Ser	Ser
1535						1540					1545			
Gly	Glu	Ile	Ala	Ile	Asp	Gln	Glu	Ser	Gln	Lys	Ile	Ala	Phe	Ala
1550						1555					1560			
Arg	Ala	Thr	Glu	Val	Thr	Phe	Gly	Glu	Glu	Val	Glu	Lys	Ser	Thr
1565						1570					1575			
Ser	Val	Thr	Tyr	Thr	Pro	Thr	Ile	Val	Pro	Ser	Ser	Ala	Ser	Ala
1580						1585					1590			
Tyr	Val	Ser	Glu	Glu	Glu	Ala	Val	Thr	Leu	Ile	Gly	Asn	Pro	Trp
1595						1600					1605			
Pro	Asp	Asp	Leu	Leu	Ser	Thr	Lys	Glu	Ser	Trp	Val	Glu	Ala	Thr
1610						1615					1620			
Pro	Arg	Gln	Val	Val	Glu	Leu	Ser	Gly	Ser	Ser	Ser	Ile	Pro	Ile
1625						1630					1635			
Thr	Glu	Gly	Ser	Gly	Glu	Ala	Glu	Glu	Asp	Glu	Asp	Thr	Met	Phe
1640						1645					1650			
Thr	Met	Val	Thr	Asp	Leu	Ser	Gln	Arg	Asn	Thr	Thr	Asp	Thr	Leu
1655						1660					1665			
Ile	Thr	Leu	Asp	Thr	Ser	Arg	Ile	Ile	Thr	Glu	Ser	Phe	Phe	Glu
1670						1675					1680			
Val	Pro	Ala	Thr	Thr	Ile	Tyr	Pro	Val	Ser	Glu	Gln	Pro	Ser	Ala
1685						1690					1695			
Lys	Val	Val	Pro	Thr	Lys	Phe	Val	Ser	Glu	Thr	Asp	Thr	Ser	Glu
1700						1705					1710			
Trp	Ile	Ser	Ser	Thr	Thr	Val	Glu	Glu	Lys	Lys	Arg	Lys	Glu	Glu
1715						1720					1725			
Glu	Gly	Thr	Thr	Gly	Thr	Ala	Ser	Thr	Phe	Glu	Val	Tyr	Ser	Ser
1730						1735					1740			
Thr	Gln	Arg	Ser	Asp	Gln	Leu	Ile	Leu	Pro	Phe	Glu	Leu	Glu	Ser
1745						1750					1755			
Pro	Asn	Val	Ala	Thr	Ser	Ser	Asp	Ser	Gly	Thr	Arg	Lys	Ser	Phe
1760						1765					1770			
Met	Ser	Leu	Thr	Thr	Pro	Thr	Gln	Ser	Glu	Arg	Glu	Met	Thr	Asp
1775						1780					1785			
Ser	Thr	Pro	Val	Phe	Thr	Glu	Thr	Asn	Thr	Leu	Glu	Asn	Leu	Gly
1790						1795					1800			
Ala	Gln	Thr	Thr	Glu	His	Ser	Ser	Ile	His	Gln	Pro	Gly	Val	Gln
1805						1810					1815			
Glu	Gly	Leu	Thr	Thr	Leu	Pro	Arg	Ser	Pro	Ala	Ser	Val	Phe	Met
1820						1825					1830			
Glu	Gln	Gly	Ser	Gly	Glu	Ala	Ala	Ala	Asp	Pro	Glu	Thr	Thr	Thr
1835						1840					1845			
Val	Ser	Ser	Phe	Ser	Leu	Asn	Val	Glu	Tyr	Ala	Ile	Gln	Ala	Glu
1850						1855					1860			
Lys	Glu	Val	Ala	Gly	Thr	Leu	Ser	Pro	His	Val	Glu	Thr	Thr	Phe
1865						1870					1875			
Ser	Thr	Glu	Pro	Thr	Gly	Leu	Val	Leu	Ser	Thr	Val	Met	Asp	Arg
1880						1885					1890			
Val	Val	Ala	Glu	Asn	Ile	Thr	Gln	Thr	Ser	Arg	Glu	Ile	Val	Ile
1895						1900					1905			
Ser	Glu	Arg	Leu	Gly	Glu	Pro	Asn	Tyr	Gly	Ala	Glu	Ile	Arg	Gly
1910						1915					1920			
Phe	Ser	Thr	Gly	Phe	Pro	Leu	Glu	Glu	Asp	Phe	Ser	Gly	Asp	Phe
1925						1930					1935			
Arg	Glu	Tyr	Ser	Thr	Val	Ser	His	Pro	Ile	Ala	Lys	Glu	Glu	Thr
1940						1945					1950			

Val	Met	Met	Glu	Gly	Ser	Gly	Asp	Ala	Ala	Phe	Arg	Asp	Thr	Gln
1955						1960					1965			
Thr	Ser	Pro	Ser	Thr	Val	Pro	Thr	Ser	Val	His	Ile	Ser	His	Ile
1970						1975					1980			
Ser	Asp	Ser	Glu	Gly	Pro	Ser	Ser	Thr	Met	Val	Ser	Thr	Ser	Ala
1985						1990					1995			
Phe	Pro	Trp	Glu	Glu	Phe	Thr	Ser	Ser	Ala	Glu	Gly	Ser	Gly	Glu
2000						2005					2010			
Gln	Leu	Val	Thr	Val	Ser	Ser	Ser	Val	Val	Pro	Val	Leu	Pro	Ser
2015						2020					2025			
Ala	Val	Gln	Lys	Phe	Ser	Gly	Thr	Ala	Ser	Ser	Ile	Ile	Asp	Glu
2030						2035					2040			
Gly	Leu	Gly	Glu	Val	Gly	Thr	Val	Asn	Glu	Ile	Asp	Arg	Arg	Ser
2045						2050					2055			
Thr	Ile	Leu	Pro	Thr	Ala	Glu	Val	Glu	Gly	Thr	Lys	Ala	Pro	Val
2060						2065					2070			
Glu	Lys	Glu	Glu	Val	Lys	Val	Ser	Gly	Thr	Val	Ser	Thr	Asn	Phe
2075						2080					2085			
Pro	Gln	Thr	Ile	Glu	Pro	Ala	Lys	Leu	Trp	Ser	Arg	Gln	Glu	Val
2090						2095					2100			
Asn	Pro	Val	Arg	Gln	Glu	Ile	Glu	Ser	Glu	Thr	Thr	Ser	Glu	Glu
2105						2110					2115			
Gln	Ile	Gln	Glu	Glu	Lys	Ser	Phe	Glu	Ser	Pro	Gln	Asn	Ser	Pro
2120						2125					2130			
Ala	Thr	Glu	Gln	Thr	Ile	Phe	Asp	Ser	Gln	Thr	Phe	Thr	Glu	Thr
2135						2140					2145			
Glu	Leu	Lys	Thr	Thr	Asp	Tyr	Ser	Val	Leu	Thr	Thr	Lys	Lys	Thr
2150						2155					2160			
Tyr	Ser	Asp	Asp	Lys	Glu	Met	Lys	Glu	Glu	Asp	Thr	Ser	Leu	Val
2165						2170					2175			
Asn	Met	Ser	Thr	Pro	Asp	Pro	Asp	Ala	Asn	Gly	Leu	Glu	Ser	Tyr
2180						2185					2190			
Thr	Thr	Leu	Pro	Glu	Ala	Thr	Glu	Lys	Ser	His	Phe	Phe	Leu	Ala
2195						2200					2205			
Thr	Ala	Leu	Val	Thr	Glu	Ser	Ile	Pro	Ala	Glu	His	Val	Val	Thr
2210						2215					2220			
Asp	Ser	Pro	Ile	Lys	Lys	Glu	Glu	Ser	Thr	Lys	His	Phe	Pro	Lys
2225						2230					2235			
Gly	Met	Arg	Pro	Thr	Ile	Gln	Glu	Ser	Asp	Thr	Glu	Leu	Leu	Phe
2240						2245					2250			
Ser	Gly	Leu	Gly	Ser	Gly	Glu	Glu	Val	Leu	Pro	Thr	Leu	Pro	Thr
2255						2260					2265			
Glu	Ser	Val	Asn	Phe	Thr	Glu	Val	Glu	Gln	Ile	Asn	Asn	Thr	Leu
2270						2275					2280			
Tyr	Pro	His	Thr	Ser	Gln	Val	Glu	Ser	Thr	Ser	Ser	Asp	Lys	Ile
2285						2290					2295			
Glu	Asp	Phe	Asn	Arg	Met	Glu	Asn	Val	Ala	Lys	Glu	Val	Gly	Pro
2300						2305					2310			
Leu	Val	Ser	Gln	Thr	Asp	Ile	Phe	Glu	Gly	Ser	Gly	Ser	Val	Thr
2315						2320					2325			
Ser	Thr	Thr	Leu	Ile	Glu	Ile	Leu	Ser	Asp	Thr	Gly	Ala	Glu	Gly
2330						2335					2340			
Pro	Thr	Val	Ala	Pro	Leu	Pro	Phe	Ser	Thr	Asp	Ile	Gly	His	Pro
2345						2350					2355			
Gln	Asn	Gln	Thr	Val	Arg	Trp	Ala	Glu	Glu	Ile	Gln	Thr	Ser	Arg
2360						2365					2370			
Pro	Gln	Thr	Ile	Thr	Glu	Gln	Asp	Ser	Asn	Lys	Asn	Ser	Ser	Thr
2375						2380					2385			
Ala	Glu	Ile	Asn	Glu	Thr	Thr	Thr	Ser	Ser	Thr	Asp	Phe	Leu	Ala
2390						2395					2400			
Arg	Ala	Tyr	Gly	Phe	Glu	Met	Ala	Lys	Glu	Phe	Val	Thr	Ser	Ala
2405						2410					2415			

Pro Lys	Pro Ser Asp Leu Tyr	Tyr Glu Pro Ser Gly	Glu Gly Ser
2420	2425	2430	
Gly Glu	Val Asp Ile Val Asp	Ser Phe His Thr Ser	Ala Thr Thr
2435	2440	2445	
Gln Ala	Thr Arg Gln Glu Ser	Ser Thr Thr Phe Val	Ser Asp Gly
2450	2455	2460	
Ser Leu	Glu Lys His Pro Glu	Val Pro Ser Ala Lys	Ala Val Thr
2465	2470	2475	
Ala Asp	Gly Phe Pro Thr Val	Ser Val Met Leu Pro	Leu His Ser
2480	2485	2490	
Glu Gln	Asn Lys Ser Ser Pro	Asp Pro Thr Ser Thr	Leu Ser Asn
2495	2500	2505	
Thr Val	Ser Tyr Glu Arg Ser	Thr Asp Gly Ser Phe	Gln Asp Arg
2510	2515	2520	
Phe Arg	Glu Phe Glu Asp Ser	Thr Leu Lys Pro Asn	Arg Lys Lys
2525	2530	2535	
Pro Thr	Glu Asn Ile Ile Ile	Asp Leu Asp Lys Glu	Asp Lys Asp
2540	2545	2550	
Leu Ile	Leu Thr Ile Thr Glu	Ser Thr Ile Leu Glu	Ile Leu Pro
2555	2560	2565	
Glu Leu	Thr Ser Asp Lys Asn	Thr Ile Ile Asp Ile	Asp His Thr
2570	2575	2580	
Lys Pro	Val Tyr Glu Asp Ile	Leu Gly Met Gln Thr	Asp Ile Asp
2585	2590	2595	
Thr Glu	Val Pro Ser Glu Pro	His Asp Ser Asn Asp	Glu Ser Asn
2600	2605	2610	
Asp Asp	Ser Thr Gln Val Glu	Glu Ile Tyr Glu Ala	Ala Val Asn
2615	2620	2625	
Leu Ser	Leu Thr Glu Glu Thr	Phe Glu Gly Ser Ala	Asp Val Leu
2630	2635	2640	
Ala Ser	Tyr Thr Gln Ala Thr	His Asp Glu Ser Met	Thr Tyr Glu
2645	2650	2655	
Asp Arg	Ser Gln Leu Asp His	Met Gly Phe His Phe	Thr Thr Gly
2660	2665	2670	
Ile Pro	Ala Pro Ser Thr Glu	Thr Glu Leu Asp Val	Leu Leu Pro
2675	2680	2685	
Thr Ala	Thr Ser Leu Pro Ile	Pro Arg Lys Ser Ala	Thr Val Ile
2690	2695	2700	
Pro Glu	Ile Glu Gly Ile Lys	Ala Glu Ala Lys Ala	Leu Asp Asp
2705	2710	2715	
Met Phe	Glu Ser Ser Thr Leu	Ser Asp Gly Gln Ala	Ile Ala Asp
2720	2725	2730	
Gln Ser	Glu Ile Ile Pro Thr	Leu Gly Gln Phe Glu	Arg Thr Gln
2735	2740	2745	
Glu Glu	Tyr Glu Asp Lys Lys	His Ala Gly Pro Ser	Phe Gln Pro
2750	2755	2760	
Glu Phe	Ser Ser Gly Ala Glu	Glu Ala Leu Val Asp	His Thr Pro
2765	2770	2775	
Tyr Leu	Ser Ile Ala Thr Thr	His Leu Met Asp Gln	Ser Val Thr
2780	2785	2790	
Glu Val	Pro Asp Val Met Glu	Gly Ser Asn Pro Pro	Tyr Tyr Thr
2795	2800	2805	
Asp Thr	Thr Leu Ala Val Ser	Thr Phe Ala Lys Leu	Ser Ser Gln
2810	2815	2820	
Thr Pro	Ser Ser Pro Leu Thr	Ile Tyr Ser Gly Ser	Glu Ala Ser
2825	2830	2835	
Gly His	Thr Glu Ile Pro Gln	Pro Ser Ala Leu Pro	Gly Ile Asp
2840	2845	2850	
Val Gly	Ser Ser Val Met Ser	Pro Gln Asp Ser Phe	Lys Glu Ile
2855	2860	2865	
His Val	Asn Ile Glu Ala Thr	Phe Lys Pro Ser Ser	Glu Glu Tyr
2870	2875	2880	



Leu	His	Ile	Thr	Glu	Pro	Pro	Ser	Leu	Ser	Pro	Asp	Thr	Lys	Leu
2885						2890					2895			
Glu	Pro	Ser	Glu	Asp	Asp	Gly	Lys	Pro	Glu	Leu	Leu	Glu	Glu	Met
2900						2905					2910			
Glu	Ala	Ser	Pro	Thr	Glu	Leu	Ile	Ala	Val	Glu	Gly	Thr	Glu	Ile
2915						2920					2925			
Leu	Gln	Asp	Phe	Gln	Asn	Lys	Thr	Asp	Gly	Gln	Val	Ser	Gly	Glu
2930						2935					2940			
Ala	Ile	Lys	Met	Phe	Pro	Thr	Ile	Lys	Thr	Pro	Glu	Ala	Gly	Thr
2945						2950					2955			
Val	Ile	Thr	Thr	Ala	Asp	Glu	Ile	Glu	Leu	Glu	Gly	Ala	Thr	Gln
2960						2965					2970			
Trp	Pro	His	Ser	Thr	Ser	Ala	Ser	Ala	Thr	Tyr	Gly	Val	Glu	Ala
2975						2980					2985			
Gly	Val	Val	Pro	Trp	Leu	Ser	Pro	Gln	Thr	Ser	Glu	Arg	Pro	Thr
2990						2995					3000			
Leu	Ser	Ser	Ser	Pro	Glu	Ile	Asn	Pro	Glu	Thr	Gln	Ala	Ala	Leu
3005						3010					3015			
Ile	Arg	Gly	Gln	Asp	Ser	Thr	Ile	Ala	Ala	Ser	Glu	Gln	Gln	Val
3020						3025					3030			
Ala	Ala	Arg	Ile	Leu	Asp	Ser	Asn	Asp	Gln	Ala	Thr	Val	Asn	Pro
3035						3040					3045			
Val	Glu	Phe	Asn	Thr	Glu	Val	Ala	Thr	Pro	Pro	Phe	Ser	Leu	Leu
3050						3055					3060			
Glu	Thr	Ser	Asn	Glu	Thr	Asp	Phe	Leu	Ile	Gly	Ile	Asn	Glu	Glu
3065						3070					3075			
Ser	Val	Glu	Gly	Thr	Ala	Ile	Tyr	Leu	Pro	Gly	Pro	Asp	Arg	Cys
3080						3085					3090			
Lys	Met	Asn	Pro	Cys	Leu	Asn	Gly	Gly	Thr	Cys	Tyr	Pro	Thr	Glu
3095						3100					3105			
Thr	Ser	Tyr	Val	Cys	Thr	Cys	Val	Pro	Gly	Tyr	Ser	Gly	Asp	Gln
3110						3115					3120			
Cys	Glu	Leu	Asp	Phe	Asp	Glu	Cys	His	Ser	Asn	Pro	Cys	Arg	Asn
3125						3130					3135			
Gly	Ala	Thr	Cys	Val	Asp	Gly	Phe	Asn	Thr	Phe	Arg	Cys	Leu	Cys
3140						3145					3150			
Leu	Pro	Ser	Tyr	Val	Gly	Ala	Leu	Cys	Glu	Gln	Asp	Thr	Glu	Thr
3155						3160					3165			
Cys	Asp	Tyr	Gly	Trp	His	Lys	Phe	Gln	Gly	Gln	Cys	Tyr	Lys	Tyr
3170						3175					3180			
Phe	Ala	His	Arg	Arg	Thr	Trp	Asp	Ala	Ala	Glu	Arg	Glu	Cys	Arg
3185						3190					3195			
Leu	Gln	Gly	Ala	His	Leu	Thr	Ser	Ile	Leu	Ser	His	Glu	Glu	Gln
3200						3205					3210			
Met	Phe	Val	Asn	Arg	Val	Gly	His	Asp	Tyr	Gln	Trp	Ile	Gly	Leu
3215						3220					3225			
Asn	Asp	Lys	Met	Phe	Glu	His	Asp	Phe	Arg	Trp	Thr	Asp	Gly	Ser
3230						3235					3240			
Thr	Leu	Gln	Tyr	Glu	Asn	Trp	Arg	Pro	Asn	Gln	Pro	Asp	Ser	Phe
3245						3250					3255			
Phe	Ser	Ala	Gly	Glu	Asp	Cys	Val	Val	Ile	Ile	Trp	His	Glu	Asn
3260						3265					3270			
Gly	Gln	Trp	Asn	Asp	Val	Pro	Cys	Asn	Tyr	His	Leu	Thr	Tyr	Thr
3275						3280					3285			
Cys	Lys	Lys	Gly	Thr	Val	Ala	Cys	Gly	Gln	Pro	Pro	Val	Val	Glu
3290						3295					3300			
Asn	Ala	Lys	Thr	Phe	Gly	Lys	Met	Lys	Pro	Arg	Tyr	Glu	Ile	Asn
3305						3310					3315			
Ser	Leu	Ile	Arg	Tyr	His	Cys	Lys	Asp	Gly	Phe	Ile	Gln	Arg	His
3320						3325					3330			
Leu	Pro	Thr	Ile	Arg	Cys	Leu	Gly	Asn	Gly	Arg	Trp	Ala	Ile	Pro
3335						3340					3345			

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Lys Ile Thr Cys Met Asn Pro Ser Ala Tyr Gln Arg Thr Tyr Ser  
 3350 3355 3360  
 Met Lys Tyr Phe Lys Asn Ser Ser Ser Ala Lys Asp Asn Ser Ile  
 3365 3370 3375  
 Asn Thr Ser Lys His Asp His Arg Trp Ser Arg Arg Trp Gln Glu  
 3380 3385 3390  
 Ser Arg Arg  
 3395

&lt;210&gt; 286

&lt;211&gt; 148

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 286

Met Met His Leu Leu Asn Ser Gln Gly Trp Asn Glu Pro Ala Gly Pro  
 1 5 10 15  
 Pro Glu Ser Trp Ser Gly Val Gln Ser Ser Val Phe Leu Ser Val Tyr  
 20 25 30  
 Ser Ser Leu Thr Val Pro Arg Pro Ser Gly Val Gly Ala Gly Ser Gln  
 35 40 45  
 Cys Trp Arg Arg Asn Asn Lys Ser Gln Leu Glu Pro Leu Phe Leu Lys  
 50 55 60  
 Ser Ala Tyr Cys Ala Gln Ile Leu Phe Lys His Trp Thr Trp Ile Leu  
 65 70 75 80  
 Ser Leu Ala Leu Ser Thr Pro Ala Val Gly Val Pro Pro Leu Pro Thr  
 85 90 95  
 Cys Asp Gly Val Gln Arg His Leu Leu Phe Cys Met Val Phe Asn Arg  
 100 105 110  
 Leu Gly Val Leu Phe Ile Ser Ser Asn Phe Val Gln Glu Leu Met Ala  
 115 120 125  
 Cys Leu Gly Leu Ser Ser Leu Asn Gln Arg Lys Trp Lys Pro Phe Pro  
 130 135 140  
 Cys Cys Ser Pro  
 145

&lt;210&gt; 287

&lt;211&gt; 449

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 287

Met Leu Trp Lys Leu Val Glu Asn Val Lys Tyr Glu Asp Ile Tyr Glu  
 1 5 10 15  
 Asp Arg His Asp Gly Val Pro Ser His Ser Ser Arg Leu Ser Gln Leu  
 20 25 30  
 Gly Ser Val Ser Gln Gly Pro Tyr Ser Ser Ala Pro Pro Leu Ser His  
 35 40 45  
 Thr Pro Ser Ser Asp Phe Gln Pro Pro Tyr Phe Pro Pro Pro Tyr Gln  
 50 55 60  
 Pro Leu Pro Tyr His Gln Ser Gln Asp Pro Tyr Ser His Val Asn Asp  
 65 70 75 80

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Pro Tyr Ser Leu Asn Pro Leu His Gln Pro Gln Gln His Pro Trp Gly  
 85 90 95  
 Gln Arg Gln Arg Gln Glu Val Gly Ser Glu Ala Gly Ser Leu Leu Pro  
 100 105 110  
 Gln Pro Arg Ala Ala Leu Pro Gln Leu Ser Gly Leu Asp Pro Arg Arg  
 115 120 125  
 Asp Tyr His Ser Val Arg Arg Pro Asp Val Leu Leu His Ser Ala His  
 130 135 140  
 His Gly Leu Asp Ala Gly Met Gly Asp Ser Leu Ser Leu His Gly Leu  
 145 150 155 160  
 Gly His Pro Gly Met Glu Asp Val Gln Ser Val Glu Asp Ala Asn Asn  
 165 170 175  
 Ser Gly Met Asn Leu Leu Asp Gln Ser Val Ile Lys Lys Val Pro Val  
 180 185 190  
 Pro Pro Lys Ser Val Thr Ser Leu Met Met Asn Lys Asp Gly Phe Leu  
 195 200 205  
 Gly Gly Met Ser Val Asn Thr Gly Glu Val Phe Cys Ser Val Pro Gly  
 210 215 220  
 Arg Leu Ser Leu Leu Ser Ser Thr Ser Lys Tyr Lys Val Thr Val Gly  
 225 230 235 240  
 Glu Val Gln Arg Arg Leu Ser Pro Pro Glu Cys Leu Asn Ala Ser Leu  
 245 250 255  
 Leu Gly Gly Val Leu Arg Arg Ala Lys Ser Lys Asn Gly Gly Arg Ser  
 260 265 270  
 Leu Arg Glu Arg Leu Glu Lys Ile Gly Leu Asn Leu Pro Ala Gly Arg  
 275 280 285  
 Arg Lys Ala Ala Asn Val Thr Leu Leu Thr Ser Leu Val Glu Gly Glu  
 290 295 300  
 Ala Val His Leu Ala Arg Asp Phe Gly Tyr Ile Cys Glu Thr Glu Phe  
 305 310 315 320  
 Pro Ala Lys Ala Val Ser Glu Tyr Leu Asn Arg Gln His Thr Asp Pro  
 325 330 335  
 Ser Asp Leu His Ser Arg Lys Asn Met Leu Leu Ala Thr Lys Gln Leu  
 340 345 350  
 Cys Lys Glu Phe Thr Asp Leu Leu Ala Gln Asp Arg Thr Pro Ile Gly  
 355 360 365  
 Asn Ser Arg Pro Ser Pro Ile Leu Glu Pro Gly Ile Gln Ser Cys Leu  
 370 375 380  
 Thr His Phe Ser Leu Ile Thr His Gly Phe Gly Ala Pro Ala Ile Cys  
 385 390 395 400  
 Ala Ala Leu Thr Ala Leu Gln Asn Tyr Leu Thr Glu Ala Leu Lys Gly  
 405 410 415  
 Met Asp Lys Met Phe Leu Asn Asn Thr Thr Thr Asn Arg His Thr Ser  
 420 425 430  
 Gly Glu Gly Pro Gly Ser Lys Thr Gly Asp Lys Glu Glu Lys His Arg  
 435 440 445  
 Lys

&lt;210&gt; 288

&lt;211&gt; 114

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 288

Met Leu Leu Ser Val Met Ala Tyr Asp Arg Phe Val Ala Ile Cys His  
 1 5 10 15

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Pro Leu Tyr His Ser Ala Ile Met Asn Pro Cys Phe Cys Gly Phe Leu  
 20. 25 30  
 Leu Leu Leu Ser Phe Phe Phe Phe Leu Ser Leu Leu Asp Thr Gln Leu  
 35 40 45  
 His Asn Leu Ile Ala Leu Gln Met Thr Cys Phe Lys Asp Val Glu Ile  
 50 55 60  
 Pro Asn Phe Phe Cys Asp Pro Ser Gln Leu Pro His Leu Ala Cys Cys  
 65 70 75 80  
 Asp Thr Phe Thr Asn Asn Ile Ile Val Tyr Phe Pro Ala Val Ile Phe  
 85 90 95  
 Val Phe Leu Pro Ile Ser Gly Thr Leu Phe Ser Leu Lys Leu Phe Pro  
 100 105 110  
 Pro Phe

&lt;210&gt; 289

&lt;211&gt; 195

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 289  
 Met Met Ala Ile Arg Glu Leu Lys Val Cys Leu Leu Gly Asp Thr Gly  
 1 5 10 15  
 Val Gly Lys Ser Ser Ile Val Cys Arg Phe Val Gln Asp His Phe Asp  
 20 25 30  
 His Asn Ile Ser Pro Thr Ile Gly Ala Ser Phe Met Thr Lys Thr Val  
 35 40 45  
 Pro Cys Gly Asn Glu Leu His Lys Phe Leu Ile Trp Asp Thr Ala Gly  
 50 55 60  
 Gln Glu Arg Phe His Ser Leu Ala Pro Met Tyr Tyr Arg Gly Ser Ala  
 65 70 75 80  
 Ala Ala Val Ile Val Tyr Asp Ile Thr Lys Gln Asp Ser Phe Tyr Thr  
 85 90 95  
 Leu Lys Lys Trp Val Lys Glu Leu Lys Glu His Gly Pro Glu Asn Ile  
 100 105 110  
 Val Met Ala Ile Ala Gly Asn Lys Cys Asp Leu Ser Asp Ile Arg Glu  
 115 120 125  
 Val Pro Leu Lys Asp Ala Lys Glu Tyr Ala Glu Ser Ile Gly Ala Ile  
 130 135 140  
 Val Val Glu Thr Ser Ala Lys Asn Ala Ile Asn Ile Glu Glu Leu Phe  
 145 150 155 160  
 Gln Gly Ile Ser Arg Gln Ile Pro Pro Leu Asp Pro His Glu Asn Gly  
 165 170 175  
 Asn Asn Gly Thr Ile Lys Val Glu Lys Pro Thr Met Gln Ala Ser Arg  
 180 185 190  
 Arg Cys Cys  
 195

&lt;210&gt; 290

&lt;211&gt; 270

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 290

Met Ala Ala Ser Ser Ser Gly Glu Lys Glu Lys Glu Arg Leu Gly Gly  
 1 5 10 15  
 Gly Leu Gly Val Ala Gly Gly Asn Ser Thr Arg Glu Arg Leu Leu Ser  
 20 25 30  
 Ala Leu Glu Asp Leu Glu Val Leu Ser Arg Glu Leu Ile Glu Met Leu  
 35 40 45  
 Ala Ile Ser Arg Asn Gln Lys Leu Leu Gln Ala Gly Glu Glu Asn Gln  
 50 55 60  
 Val Leu Glu Leu Leu Ile His Arg Asp Gly Glu Phe Gln Glu Leu Met  
 65 70 75 80  
 Lys Leu Ala Leu Asn Gln Gly Lys Ile His His Glu Met Gln Val Leu  
 85 90 95  
 Glu Lys Glu Val Glu Lys Arg Asp Ser Asp Ile Gln Gln Leu Gln Lys  
 100 105 110  
 Gln Leu Lys Glu Ala Glu Gln Ile Leu Ala Thr Ala Val Tyr Gln Ala  
 115 120 125  
 Lys Glu Lys Leu Lys Ser Ile Glu Lys Ala Arg Lys Gly Ala Ile Ser  
 130 135 140  
 Ser Glu Glu Ile Ile Lys Tyr Ala His Arg Ile Ser Ala Ser Asn Ala  
 145 150 155 160  
 Val Cys Ala Pro Leu Thr Trp Val Pro Gly Asp Pro Arg Arg Pro Tyr  
 165 170 175  
 Pro Thr Asp Leu Glu Met Arg Ser Gly Leu Leu Gly Gln Met Asn Asn  
 180 185 190  
 Pro Ser Thr Asn Gly Val Asn Gly His Leu Pro Gly Asp Ala Leu Ala  
 195 200 205  
 Ala Gly Arg Leu Pro Asp Val Leu Ala Pro Gln Tyr Pro Trp Gln Ser  
 210 215 220  
 Asn Asp Met Ser Met Asn Met Leu Pro Pro Asn His Ser Ser Asp Phe  
 225 230 235 240  
 Leu Leu Glu Pro Pro Gly His Asn Lys Glu Asn Glu Asp Asp Val Glu  
 245 250 255  
 Ile Met Ser Thr Asp Ser Ser Ser Ser Ser Ser Glu Ser Asp  
 260 265 270

&lt;210&gt; 291

&lt;211&gt; 228

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 291

Met Leu Ser Arg Cys Arg Ser Gly Leu Leu His Val Leu Gly Leu Ser  
 1 5 10 15  
 Phe Leu Leu Gln Thr Arg Arg Pro Ile Leu Leu Cys Ser Pro Arg Leu  
 20 25 30  
 Met Lys Pro Leu Val Val Phe Val Leu Gly Gly Pro Gly Ala Gly Lys  
 35 40 45  
 Gly Thr Gln Cys Ala Arg Ile Val Glu Lys Tyr Gly Tyr Thr His Leu  
 50 55 60  
 Ser Ala Gly Glu Leu Leu Arg Asp Glu Arg Lys Asn Pro Asp Ser Gln  
 65 70 75 80  
 Tyr Gly Glu Leu Ile Glu Lys Tyr Ile Lys Glu Gly Lys Ile Val Pro  
 85 90 95  
 Val Glu Ile Thr Ile Ser Leu Leu Lys Arg Glu Met Asp Gln Thr Met  
 100 105 110

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Ala Ala Asn Ala Gln Lys Asn Lys Phe Leu Ile Asp Gly Phe Pro Arg  
 115 120 125  
 Asn Gln Asp Asn Leu Gln Gly Trp Asn Lys Thr Met Asp Gly Lys Ala  
 130 135 140  
 Asp Val Ser Phe Val Leu Phe Phe Asp Cys Asn Asn Glu Ile Cys Ile  
 145 150 155 160  
 Glu Arg Cys Leu Glu Arg Gly Lys Ser Ser Gly Arg Ser Asp Asp Asn  
 165 170 175  
 Arg Glu Ser Leu Glu Lys Arg Ile Gln Thr Tyr Leu Gln Ser Thr Lys  
 180 185 190  
 Pro Ile Ile Asp Leu Tyr Glu Glu Met Gly Lys Val Lys Lys Ile Asp  
 195 200 205  
 Ala Ser Lys Ser Val Asp Glu Val Phe Asp Glu Val Val Gln Ile Phe  
 210 215 220  
 Asp Lys Glu Gly  
 225

&lt;210&gt; 292

&lt;211&gt; 130

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 292  
 Met Ala Phe Cys Leu Arg Ala Ser Leu Gly Pro Asp Cys Cys Cys Trp  
 1 5 10 15  
 Tyr Gln Ser Pro Glu Thr Leu Pro Pro Trp Ser Pro Cys Met Pro Ser  
 20 25 30  
 Cys Ser Tyr Cys Leu Val Ala Leu Lys Gln His Ile Ser Thr Val Pro  
 35 40 45  
 Gly Arg Ile Val Gly Gly Phe Thr Thr Pro Ala Phe Leu Thr Ser Ser  
 50 55 60  
 Ser Ala Gln His Trp Val Pro Leu Pro Ser Phe Pro Ala Gly Ala Ser  
 65 70 75 80  
 Trp Ala Thr Val Ser Gly Ser Gly Pro Ala Arg Val Val Leu Leu Phe  
 85 90 95  
 Leu Leu Leu Leu Gly Asn His Thr Trp Gln Val Lys Cys Pro Lys His  
 100 105 110  
 Leu Val Ser Leu Pro Lys Asn Lys Pro Phe Leu Cys Thr Ser Leu Glu  
 115 120 125  
 Ala Arg  
 130

&lt;210&gt; 293

&lt;211&gt; 460

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 293  
 Met Ala Ser Leu Leu Gln Ser Asp Arg Val Leu Tyr Leu Val Gln Gly  
 1 5 10 15  
 Glu Lys Lys Val Arg Ala Pro Leu Ser Gln Leu Tyr Phe Cys Arg Tyr  
 20 25 30

Cys Ser Glu Leu Arg Ser Leu Glu Cys Val Ser His Glu Val Asp Ser  
 35 40 45  
 His Tyr Cys Pro Ser Cys Leu Glu Asn Met Pro Ser Ala Glu Ala Lys  
 50 55 60  
 Leu Lys Lys Asn Arg Cys Ala Asn Cys Phe Asp Cys Pro Gly Cys Met  
 65 70 75 80  
 His Thr Leu Ser Thr Arg Ala Thr Ser Ile Ser Thr Gln Leu Pro Asp  
 85 90 95  
 Asp Pro Ala Lys Thr Thr Met Lys Lys Ala Tyr Tyr Leu Ala Cys Gly  
 100 105 110  
 Phe Cys Arg Trp Thr Ser Arg Asp Val Gly Met Ala Asp Lys Ser Val  
 115 120 125  
 Ala Ser Gly Gly Trp Gln Glu Pro Glu Asn Pro His Thr Gln Arg Met  
 130 135 140  
 Asn Lys Leu Ile Glu Tyr Tyr Gln Gln Leu Ala Gln Lys Glu Lys Val  
 145 150 155 160  
 Glu Arg Asp Arg Lys Lys Leu Ala Arg Arg Asn Tyr Met Pro Leu  
 165 170 175  
 Ala Phe Ser Asp Lys Tyr Gly Leu Gly Thr Arg Leu Gln Arg Pro Arg  
 180 185 190  
 Ala Gly Ala Ser Ile Ser Thr Leu Ala Gly Leu Ser Leu Lys Glu Gly  
 195 200 205  
 Glu Asp Gln Lys Glu Ile Lys Ile Glu Pro Ala Gln Ala Val Asp Glu  
 210 215 220  
 Val Glu Pro Leu Pro Glu Asp Tyr Tyr Thr Arg Pro Val Asn Leu Thr  
 225 230 235 240  
 Glu Val Thr Thr Leu Gln Gln Arg Leu Leu Gln Pro Asp Phe Gln Pro  
 245 250 255  
 Val Cys Ala Ser Gln Leu Tyr Pro Arg His Lys His Leu Leu Ile Lys  
 260 265 270  
 Arg Ser Leu Arg Cys Arg Lys Cys Glu His Asn Leu Ser Lys Pro Glu  
 275 280 285  
 Phe Asn Pro Thr Ser Ile Lys Phe Lys Ile Gln Leu Val Ala Val Asn  
 290 295 300  
 Tyr Ile Pro Glu Val Arg Ile Met Ser Ile Pro Asn Leu Arg Tyr Met  
 305 310 315 320  
 Lys Glu Ser Gln Val Leu Leu Thr Leu Thr Asn Pro Val Glu Asn Leu  
 325 330 335  
 Thr His Val Thr Leu Phe Glu Cys Glu Gly Asp Pro Asp Asp Ile  
 340 345 350  
 Asn Ser Thr Ala Lys Val Val Val Pro Pro Lys Glu Leu Val Leu Ala  
 355 360 365  
 Gly Lys Asp Ala Ala Ala Glu Tyr Asp Glu Leu Ala Glu Pro Gln Asp  
 370 375 380  
 Phe Gln Asp Asp Pro Asp Ile Ile Ala Phe Arg Lys Ala Asn Lys Val  
 385 390 395 400  
 Gly Ile Phe Ile Lys Val Thr Pro Gln Arg Glu Glu Gly Glu Val Thr  
 405 410 415  
 Val Cys Phe Lys Met Lys His Asp Phe Lys Asn Leu Ala Ala Pro Ile  
 420 425 430  
 Arg Pro Ile Glu Glu Ser Asp Gln Gly Thr Glu Val Ile Trp Leu Thr  
 435 440 445  
 Gln His Val Glu Leu Ser Leu Gly Pro Leu Leu Pro  
 450 455 460

&lt;210&gt; 294

&lt;211&gt; 524

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 294

Met	Thr	Ala	Glu	Asp	Ser	Thr	Ala	Ala	Met	Ser	Ser	Asp	Ser	Ala	Ala		
1				5					10					15			
Gly	Ser	Ser	Ala	Lys	Val	Pro	Glu	Gly	Val	Ala	Gly	Ala	Pro	Asn	Glu		
			20					25					30				
Ala	Ala	Leu	Leu	Ala	Leu	Met	Glu	Arg	Thr	Gly	Tyr	Ser	Met	Val	Gln		
		35					40					45					
Glu	Asn	Gly	Gln	Arg	Lys	Tyr	Gly	Gly	Pro	Pro	Pro	Gly	Trp	Glu	Gly		
	50				55						60						
Pro	His	Pro	Gln	Arg	Gly	Cys	Glu	Val	Phe	Val	Gly	Lys	Ile	Pro	Arg		
65				70					75						80		
Asp	Val	Tyr	Glu	Asp	Glu	Leu	Val	Pro	Val	Phe	Glu	Ala	Val	Gly	Arg		
				85					90					95			
Thr	Tyr	Glu	Leu	Arg	Leu	Met	Met	Asp	Phe	Asp	Gly	Lys	Asn	Arg	Gly		
			100					105					110				
Tyr	Ala	Phe	Val	Met	Tyr	Cys	His	Lys	His	Glu	Ala	Lys	Arg	Ala	Val		
		115					120					125					
Arg	Glu	Leu	Asn	Asn	Tyr	Glu	Ile	Arg	Pro	Gly	Arg	Leu	Leu	Gly	Val		
	130					135					140						
Cys	Cys	Ser	Val	Asp	Asn	Cys	Arg	Leu	Phe	Ile	Gly	Gly	Ile	Pro	Lys		
145				150					155						160		
Met	Lys	Lys	Arg	Glu	Ile	Leu	Glu	Glu	Ile	Ala	Lys	Val	Thr	Glu			
				165					170					175			
Gly	Val	Leu	Asp	Val	Ile	Val	Tyr	Ala	Ser	Ala	Ala	Asp	Lys	Met	Lys		
			180					185					190				
Asn	Arg	Gly	Phe	Ala	Phe	Val	Glu	Tyr	Glu	Ser	His	Arg	Ala	Ala	Ala		
		195					200					205					
Met	Ala	Arg	Arg	Lys	Leu	Met	Pro	Gly	Arg	Ile	Gln	Leu	Trp	Gly	His		
	210				215						220						
Gln	Ile	Ala	Val	Asp	Trp	Ala	Glu	Pro	Glu	Ile	Asp	Val	Asp	Glu	Asp		
225				230						235				240			
Val	Met	Glu	Thr	Val	Lys	Ile	Leu	Tyr	Val	Arg	Asn	Leu	Met	Ile	Glu		
				245					250					255			
Thr	Thr	Glu	Asp	Thr	Ile	Lys	Lys	Ser	Phe	Gly	Gln	Phe	Asn	Pro	Gly		
			260					265					270				
Cys	Val	Glu	Arg	Val	Lys	Lys	Ile	Arg	Asp	Tyr	Ala	Phe	Val	His	Phe		
		275					280					285					
Thr	Ser	Arg	Glu	Asp	Ala	Val	His	Ala	Met	Asn	Asn	Leu	Asn	Gly	Thr		
		290				295					300						
Glu	Leu	Glu	Gly	Ser	Cys	Leu	Glu	Val	Thr	Leu	Ala	Lys	Pro	Val	Asp		
305				310					315					320			
Lys	Glu	Gln	Tyr	Ser	Arg	Tyr	Gln	Lys	Ala	Ala	Arg	Gly	Gly	Gly	Ala		
				325					330					335			
Ala	Glu	Ala	Ala	Gln	Gln	Pro	Ser	Tyr	Val	Tyr	Ser	Cys	Asp	Pro	Tyr		
			340					345					350				
Thr	Leu	Ala	Tyr	Tyr	Gly	Tyr	Pro	Tyr	Asn	Ala	Leu	Ile	Gly	Pro	Asn		
		355					360					365					
Arg	Asp	Tyr	Phe	Val	Lys	Val	Ala	Ile	Pro	Ala	Ile	Gly	Ala	Gln	Tyr		
	370					375					380						
Ser	Met	Phe	Pro	Ala	Ala	Pro	Ala	Pro	Lys	Met	Ile	Glu	Asp	Gly	Lys		
385					390					395					400		



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Ile His Thr Val Glu His Met Ile Ser Pro Ile Ala Val Gln Pro Asp  
 405 410 415  
 Pro Ala Ser Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala  
 420 425 430  
 Ala Val Ile Pro Thr Val Ser Thr Pro Pro Phe Gln Gly Arg Pro  
 435 440 445  
 Ile Thr Pro Val Tyr Thr Val Ala Pro Asn Val Gln Arg Ile Pro Thr  
 450 455 460  
 Ala Gly Ile Tyr Gly Ala Ser Tyr Val Pro Phe Ala Ala Pro Ala Thr  
 465 470 475 480  
 Ala Thr Ile Ala Thr Leu Gln Lys Asn Ala Ala Ala Ala Ala Val  
 485 490 495  
 Tyr Gly Gly Tyr Ala Gly Tyr Ile Pro Gln Ala Phe Pro Ala Ala Ala  
 500 505 510  
 Ile Gln Val Pro Ile Pro Asp Val Tyr Gln Thr Tyr  
 515 520

&lt;210&gt; 295

&lt;211&gt; 1232

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 295

Met Lys Glu Glu Val Lys Gly Ile Pro Val Arg Val Ala Leu Arg Cys  
 1 5 10 15  
 Arg Pro Leu Val Pro Lys Glu Ile Ser Glu Gly Cys Gln Met Cys Leu  
 20 25 30  
 Ser Phe Val Pro Gly Glu Pro Gln Val Val Val Gly Thr Asp Lys Ser  
 35 40 45  
 Phe Thr Tyr Asp Phe Val Phe Asp Pro Ser Thr Glu Gln Glu Glu Val  
 50 55 60  
 Phe Asn Thr Ala Val Ala Pro Leu Ile Lys Gly Val Phe Lys Gly Tyr  
 65 70 75 80  
 Asn Ala Thr Val Leu Ala Tyr Gly Gln Thr Gly Ser Gly Lys Thr Tyr  
 85 90 95  
 Ser Met Gly Gly Ala Tyr Thr Ala Glu Gln Glu Asn Glu Pro Thr Val  
 100 105 110  
 Gly Val Ile Pro Arg Val Ile Gln Leu Leu Phe Lys Glu Ile Asp Lys  
 115 120 125  
 Lys Ser Asp Phe Glu Phe Thr Leu Lys Val Ser Tyr Leu Glu Ile Tyr  
 130 135 140  
 Asn Glu Glu Ile Leu Asp Leu Leu Cys Pro Ser Arg Glu Lys Ala Gln  
 145 150 155 160  
 Ile Asn Ile Arg Glu Asp Pro Lys Glu Gly Ile Lys Ile Val Gly Leu  
 165 170 175  
 Thr Glu Lys Thr Val Leu Val Ala Leu Asp Thr Val Ser Cys Leu Glu  
 180 185 190  
 Gln Gly Asn Asn Ser Arg Thr Val Ala Ser Thr Ala Met Asn Ser Gln  
 195 200 205  
 Ser Ser Arg Ser His Ala Ile Phe Thr Ile Ser Leu Glu Gln Gly Lys  
 210 215 220  
 Lys Ser Asp Lys Asn Ser Ser Phe Arg Ser Lys Leu His Leu Val Asp  
 225 230 235 240  
 Leu Ala Gly Ser Glu Arg Gln Lys Lys Thr Lys Ala Glu Gly Asp Arg  
 245 250 255  
 Leu Lys Glu Gly Ile Asn Ile Asn Arg Gly Leu Leu Cys Leu Gly Asn  
 260 265 270

Val	Ile	Ser	Ala	Leu	Gly	Asp	Asp	Lys	Lys	Gly	Gly	Phe	Ala	Pro	Tyr
		275					280					285			
Arg	Asp	Ser	Lys	Leu	Thr	Arg	Leu	Leu	Gln	Asp	Ser	Leu	Gly	Gly	Asn
	290					295					300				
Ser	His	Thr	Leu	Met	Ile	Ala	Cys	Val	Ser	Pro	Ala	Asp	Ser	Asn	Leu
305					310					315					320
Glu	Glu	Thr	Leu	Asn	Thr	Leu	Arg	Tyr	Ala	Asp	Arg	Ala	Arg	Lys	Ile
				325					330					335	
Lys	Asn	Lys	Pro	Ile	Val	Asn	Ile	Asp	Pro	Gln	Thr	Ala	Glu	Leu	Asn
			340					345					350		
His	Leu	Lys	Gln	Gln	Val	Gln	Gln	Leu	Gln	Val	Leu	Leu	Leu	Gln	Ala
		355					360					365			
His	Gly	Gly	Thr	Leu	Pro	Gly	Ser	Ile	Thr	Val	Glu	Pro	Ser	Glu	Asn
	370					375					380				
Leu	Gln	Ser	Leu	Met	Glu	Lys	Asn	Gln	Ser	Leu	Val	Glu	Glu	Asn	Glu
385					390					395					400
Lys	Leu	Ser	Arg	Gly	Leu	Ser	Glu	Ala	Ala	Gly	Gln	Thr	Ala	Gln	Met
				405				410						415	
Leu	Glu	Arg	Ile	Ile	Trp	Thr	Glu	Gln	Ala	Asn	Glu	Lys	Met	Asn	Ala
			420					425					430		
Lys	Leu	Glu	Glu	Leu	Arg	Gln	His	Ala	Ala	Cys	Lys	Leu	Asp	Leu	Gln
		435					440					445			
Lys	Leu	Val	Glu	Thr	Leu	Glu	Asp	Gln	Glu	Leu	Lys	Glu	Asn	Val	Glu
	450					455					460				
Ile	Ile	Cys	Asn	Leu	Gln	Gln	Leu	Ile	Thr	Gln	Leu	Ser	Asp	Glu	Thr
465					470					475					480
Val	Ala	Cys	Met	Ala	Ala	Ala	Ile	Asp	Thr	Ala	Val	Glu	Gln	Glu	Ala
			485					490						495	
Gln	Val	Glu	Thr	Ser	Pro	Glu	Thr	Ser	Arg	Ser	Ser	Asp	Ala	Phe	Thr
			500					505					510		
Thr	Gln	His	Ala	Leu	Arg	Gln	Ala	Gln	Met	Ser	Lys	Glu	Leu	Val	Glu
		515					520					525			
Leu	Asn	Lys	Ala	Leu	Ala	Leu	Lys	Glu	Ala	Leu	Ala	Arg	Lys	Met	Thr
	530					535					540				
Gln	Asn	Asp	Ser	Gln	Leu	Gln	Pro	Ile	Gln	Tyr	Gln	Tyr	Gln	Asp	Asn
545					550					555					560
Ile	Lys	Glu	Pro	Glu	Leu	Glu	Val	Ile	Asn	Leu	Gln	Lys	Glu	Lys	Glu
				565					570					575	
Glu	Leu	Val	Leu	Glu	Leu	Gln	Thr	Ala	Lys	Lys	Asp	Ala	Asn	Gln	Ala
			580					585					590		
Lys	Leu	Ser	Glu	Arg	Arg	Arg	Lys	Arg	Leu	Gln	Glu	Leu	Glu	Gly	Gln
		595					600					605			
Ile	Ala	Asp	Leu	Lys	Lys	Lys	Leu	Asn	Glu	Gln	Ser	Lys	Leu	Leu	Lys
	610					615					620				
Leu	Lys	Glu	Ser	Thr	Glu	Arg	Thr	Val	Ser	Lys	Leu	Asn	Gln	Glu	Ile
625					630					635					640
Arg	Met	Met	Lys	Asn	Gln	Arg	Val	Gln	Leu	Met	Arg	Gln	Met	Lys	Glu
				645					650					655	
Asp	Ala	Glu	Lys	Phe	Arg	Gln	Trp	Lys	Gln	Lys	Arg	Asp	Lys	Glu	Val
			660					665					670		
Ile	Gln	Leu	Lys	Glu	Arg	Asp	Arg	Lys	Arg	Gln	Tyr	Glu	Leu	Leu	Lys
		675					680					685			
Leu	Glu	Arg	Asn	Phe	Gln	Lys	Gln	Ser	Asn	Val	Leu	Arg	Arg	Lys	Thr
	690					695					700				
Glu	Glu	Ala	Ala	Ala	Ala	Asn	Lys	Arg	Leu	Lys	Asp	Ala	Leu	Gln	Lys
705					710					715					720
Gln	Arg	Glu	Val	Ala	Asp	Lys	Arg	Lys	Glu	Thr	Gln	Ser	Arg	Gly	Met
				725					730					735	
Glu	Gly	Thr	Ala	Ala	Arg	Val	Lys	Asn	Trp	Leu	Gly	Asn	Glu	Ile	Glu
			740					745					750		
Val	Met	Val	Ser	Thr	Glu	Glu	Ala	Lys	Arg	His	Leu	Asn	Asp	Leu	Leu
		755					760					765			

Glu	Asp	Arg	Lys	Ile	Leu	Ala	Gln	Asp	Val	Ala	Gln	Leu	Lys	Glu	Lys
770						775					780				
Lys	Glu	Ser	Gly	Glu	Asn	Pro	Pro	Pro	Lys	Leu	Arg	Arg	Arg	Thr	Phe
785					790					795					800
Ser	Leu	Thr	Glu	Val	Arg	Gly	Gln	Val	Ser	Glu	Ser	Glu	Asp	Ser	Ile
				805					810						
Thr	Lys	Gln	Ile	Glu	Ser	Leu	Glu	Thr	Glu	Met	Glu	Phe	Arg	Ser	Ala
			820					825							
Gln	Ile	Ala	Asp	Leu	Gln	Gln	Lys	Leu	Leu	Asp	Ala	Glu	Ser	Glu	Asp
		835					840					845			
Arg	Pro	Lys	Gln	Arg	Trp	Glu	Asn	Ile	Ala	Thr	Ile	Leu	Glu	Ala	Lys
		850				855					860				
Cys	Ala	Leu	Lys	Tyr	Leu	Ile	Gly	Glu	Leu	Val	Ser	Ser	Lys	Ile	Gln
865					870					875					880
Val	Ser	Lys	Leu	Glu	Ser	Ser	Leu	Lys	Gln	Ser	Lys	Thr	Ser	Cys	Ala
				885					890						895
Asp	Met	Gln	Lys	Met	Leu	Phe	Glu	Glu	Arg	Asn	His	Phe	Ala	Glu	Ile
			900					905							
Glu	Thr	Glu	Leu	Gln	Ala	Glu	Leu	Val	Arg	Met	Glu	Gln	Gln	His	Gln
			915					920							
Glu	Lys	Val	Leu	Tyr	Leu	Leu	Ser	Gln	Leu	Gln	Gln	Ser	Gln	Met	Ala
			930			935						940			
Glu	Lys	Gln	Leu	Glu	Glu	Ser	Val	Ser	Glu	Lys	Glu	Gln	Gln	Leu	Leu
945					950					955					960
Ser	Thr	Leu	Lys	Cys	Gln	Asp	Glu	Glu	Leu	Glu	Lys	Met	Arg	Glu	Val
				965					970						975
Cys	Glu	Gln	Asn	Gln	Gln	Leu	Leu	Arg	Glu	Asn	Glu	Ile	Ile	Lys	Gln
			980					985							990
Lys	Leu	Thr	Leu	Leu	Gln	Val	Ala	Ser	Arg	Gln	Lys	His	Leu	Pro	Lys
		995					1000								
Asp	Thr	Leu	Leu	Ser	Pro	Asp	Ser	Ser	Phe	Glu	Tyr	Val	Gln	Pro	
						1015						1020			
Lys	Pro	Lys	Pro	Ser	Arg	Val	Lys	Glu	Lys	Phe	Leu	Glu	Gln	Ser	
						1030						1035			
Met	Asp	Ile	Glu	Asp	Leu	Lys	Tyr	Cys	Ser	Glu	His	Ser	Val	Asn	
						1045						1050			
Glu	His	Glu	Asp	Gly	Asp	Gly	Asp	Asp	Asp	Glu	Gly	Asp	Asp	Glu	
						1060						1065			
Glu	Trp	Lys	Pro	Thr	Lys	Leu	Val	Asn	Val	Ser	Arg	Lys	Asn	Ile	
						1075						1080			
Gln	Gly	Cys	Ser	Cys	Lys	Gly	Trp	Cys	Gly	Asn	Lys	Gln	Cys	Gly	
						1090						1095			
Cys	Arg	Lys	Gln	Lys	Ser	Asp	Cys	Gly	Val	Asp	Cys	Cys	Cys	Asp	
						1105						1110			
Pro	Thr	Lys	Cys	Arg	Asn	Arg	Gln	Gln	Gly	Lys	Asp	Ser	Leu	Gly	
						1120						1125			
Thr	Val	Glu	Arg	Thr	Gln	Asp	Ser	Glu	Ser	Ser	Phe	Lys	Leu	Glu	
						1135						1140			
Asp	Pro	Thr	Glu	Val	Thr	Pro	Gly	Leu	Ser	Phe	Phe	Asn	Pro	Val	
						1150						1155			
Cys	Ala	Thr	Pro	Asn	Ser	Lys	Ile	Leu	Lys	Glu	Met	Cys	Asp	Val	
						1165						1170			
Glu	Gln	Val	Leu	Ser	Lys	Lys	Thr	Pro	Pro	Ala	Pro	Ser	Pro	Phe	
						1180						1185			
Asp	Leu	Pro	Glu	Leu	Lys	His	Val	Ala	Thr	Glu	Tyr	Gln	Glu	Asn	
						1195						1200			
Lys	Ala	Pro	Gly	Lys	Lys	Lys	Lys	Arg	Ala	Leu	Ala	Ser	Asn	Thr	
						1210						1215			
Ser	Phe	Phe	Ser	Gly	Cys	Ser	Pro	Ile	Glu	Glu	Glu	Ala	His		
						1225						1230			

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&lt;210&gt; 296

&lt;211&gt; 230

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 296

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Met Ala Gln Gly Leu Ile Glu Val Glu Arg Lys Phe Leu Pro Gly Pro
1      5      10      15
Gly Thr Glu Glu Arg Leu Gln Glu Leu Gly Gly Thr Leu Glu Tyr Arg
20      25      30
Val Thr Phe Arg Asp Thr Tyr Tyr Asp Thr Pro Glu Leu Ser Leu Met
35      40      45
Gln Ala Asp His Trp Leu Arg Arg Arg Glu Asp Ser Gly Trp Glu Leu
50      55      60
Lys Cys Pro Gly Ala Ala Gly Val Leu Gly Pro His Thr Glu Tyr Lys
65      70      75      80
Glu Leu Thr Ala Glu Pro Thr Ile Val Ala Gln Leu Cys Lys Val Leu
85      90      95
Arg Ala Asp Gly Leu Gly Ala Gly Asp Val Ala Ala Val Leu Gly Pro
100      105      110
Leu Gly Leu Gln Glu Val Ala Ser Phe Val Thr Lys Arg Ser Ala Trp
115      120      125
Lys Leu Val Leu Leu Gly Ala Asp Glu Glu Glu Pro Gln Leu Arg Val
130      135      140
Asp Leu Asp Thr Ala Asp Phe Gly Tyr Ala Val Gly Glu Val Glu Ala
145      150      155      160
Leu Val His Glu Glu Ala Glu Val Pro Thr Ala Leu Glu Lys Ile His
165      170      175
Arg Leu Ser Ser Met Leu Gly Val Pro Ala Gln Glu Thr Ala Pro Ala
180      185      190
Lys Leu Ile Val Tyr Leu Gln Arg Phe Arg Pro Gln Asp Tyr Gln Arg
195      200      205
Leu Leu Glu Val Asn Ser Ser Arg Glu Arg Pro Gln Glu Thr Glu Asp
210      215      220
Pro Asp His Cys Leu Gly
225      230

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&lt;210&gt; 297

&lt;211&gt; 329

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 297

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Met Ser Gly Val Val Pro Thr Ala Pro Glu Gln Pro Ala Gly Glu Met
1      5      10      15
Glu Asn Gln Thr Lys Pro Pro Asp Pro Arg Pro Asp Ala Pro Pro Glu
20      25      30
Tyr Ser Ser His Phe Leu Pro Gly Pro Pro Gly Thr Ala Val Pro Pro
35      40      45
Pro Thr Gly Tyr Pro Gly Gly Leu Pro Met Gly Tyr Tyr Ser Pro Gln
50      55      60

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Gln Pro Ser Thr Phe Pro Leu Tyr Gln Pro Val Gly Gly Ile His Pro  
 65 70 75 80  
 Val Arg Tyr Gln Pro Gly Lys Tyr Pro Met Pro Asn Gln Ser Val Pro  
 85 90 95  
 Ile Thr Trp Met Pro Gly Pro Thr Pro Met Ala Asn Cys Pro Pro Gly  
 100 105 110  
 Leu Glu Tyr Leu Val Gln Leu Asp Asn Ile His Val Leu Gln His Phe  
 115 120 125  
 Glu Pro Leu Glu Met Met Thr Cys Phe Glu Thr Asn Asn Arg Tyr Asp  
 130 135 140  
 Ile Lys Asn Asn Ser Asp Gln Met Val Tyr Val Thr Glu Asp Thr  
 145 150 155 160  
 Asp Asp Phe Thr Arg Asn Ala Tyr Arg Thr Leu Arg Pro Phe Val Leu  
 165 170 175  
 Arg Val Thr Asp Cys Met Gly Arg Glu Ile Met Thr Met Gln Arg Pro  
 180 185 190  
 Phe Arg Cys Thr Cys Cys Cys Phe Cys Cys Pro Ser Ala Arg Gln Glu  
 195 200 205  
 Leu Glu Val Gln Cys Pro Pro Gly Val Thr Ile Gly Phe Val Ala Glu  
 210 215 220  
 His Trp Asn Leu Cys Arg Ala Val Tyr Ser Ile Gln Asn Glu Lys Lys  
 225 230 235 240  
 Glu Asn Val Met Arg Val Arg Gly Pro Cys Ser Thr Tyr Gly Cys Gly  
 245 250 255  
 Ser Asp Ser Val Phe Glu Val Lys Ser Leu Asp Gly Ile Ser Asn Ile  
 260 265 270  
 Gly Ser Ile Arg Lys Trp Asn Gly Leu Leu Ser Ala Met Ala Asp  
 275 280 285  
 Ala Asp His Phe Asp Ile His Phe Pro Leu Asp Leu Asp Val Lys Met  
 290 295 300  
 Lys Ala Met Ile Phe Gly Ala Cys Phe Leu Ile Asp Phe Met Tyr Phe  
 305 310 315 320  
 Glu Arg Ser Pro Pro Gln Arg Ser Arg  
 325

&lt;210&gt; 298

&lt;211&gt; 323

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 298

Met Gly Gly Gln Val Ser Ala Ser Asn Ser Phe Ser Arg Leu His Cys  
 1 5 10 15  
 Arg Asn Ala Asn Glu Asp Trp Met Ser Ala Leu Cys Pro Arg Leu Trp  
 20 25 30  
 Asp Val Pro Leu His His Leu Ser Ile Pro Gly Ser His Asp Thr Met  
 35 40 45  
 Thr Tyr Cys Leu Asn Lys Lys Ser Pro Ile Ser His Glu Glu Ser Arg  
 50 55 60  
 Leu Leu Gln Leu Leu Asn Lys Ala Leu Pro Cys Ile Thr Arg Pro Val  
 65 70 75 80  
 Val Leu Lys Trp Ser Val Thr Gln Ala Leu Asp Val Thr Glu Gln Leu  
 85 90 95  
 Asp Ala Gly Val Arg Tyr Leu Asp Leu Arg Ile Ala His Met Leu Glu  
 100 105 110  
 Gly Ser Glu Lys Asn Leu His Phe Val His Met Val Tyr Thr Thr Ala  
 115 120 125

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Leu Val Glu Asp Thr Leu Thr Glu Ile Ser Glu Trp Leu Glu Arg His  
 130 135 140  
 Pro Arg Glu Val Val Ile Leu Ala Cys Arg Asn Phe Glu Gly Leu Ser  
 145 150 155 160  
 Glu Asp Leu His Glu Tyr Leu Val Ala Cys Ile Lys Asn Ile Phe Gly  
 165 170 175  
 Asp Met Leu Cys Pro Arg Gly Glu Val Pro Thr Leu Arg Gln Leu Trp  
 180 185 190  
 Ser Arg Gly Gln Gln Val Ile Val Ser Tyr Glu Asp Glu Ser Ser Leu  
 195 200 205  
 Arg Arg His His Glu Leu Trp Pro Gly Val Pro Tyr Trp Trp Gly Asn  
 210 215 220  
 Arg Val Lys Thr Glu Ala Leu Ile Arg Tyr Leu Glu Thr Met Lys Ser  
 225 230 235 240  
 Cys Gly Arg Pro Gly Gly Leu Phe Val Ala Gly Ile Asn Leu Thr Glu  
 245 250 255  
 Asn Leu Gln Tyr Val Leu Ala His Pro Ser Glu Ser Leu Glu Lys Met  
 260 265 270  
 Thr Leu Pro Asn Leu Pro Arg Leu Ser Ala Trp Val Arg Glu Gln Cys  
 275 280 285  
 Pro Gly Pro Gly Ser Arg Cys Thr Asn Ile Ile Ala Gly Asp Phe Ile  
 290 295 300  
 Gly Ala Asp Gly Phe Val Ser Asp Val Ile Ala Leu Asn Gln Lys Leu  
 305 310 315 320  
 Leu Trp Cys

&lt;210&gt; 299

&lt;211&gt; 103

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 299

Met Thr Thr Glu Ile Gly Trp Trp Lys Leu Thr Phe Leu Arg Lys Lys  
 1 5 10 15  
 Lys Ser Thr Pro Lys Val Leu Tyr Glu Ile Pro Asp Thr Tyr Ala Gln  
 20 25 30  
 Thr Glu Gly Asp Ala Glu Pro Pro Arg Pro Asp Ala Gly Gly Pro Asn  
 35 40 45  
 Ser Asp Phe Asn Thr Arg Leu Glu Lys Ile Val Asp Lys Ser Thr Lys  
 50 55 60  
 Gly Lys His Val Lys Val Ser Asn Ser Gly Arg Phe Lys Glu Lys Lys  
 65 70 75 80  
 Lys Val Arg Ala Thr Leu Ala Glu Asn Pro Asn Leu Phe Asp Asp His  
 85 90 95  
 Glu Glu Gly Arg Ser Ser Lys  
 100

&lt;210&gt; 300

&lt;211&gt; 999

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 300  
 Met Gly Val Ala Gly Arg Asn Arg Pro Gly Ala Ala Trp Ala Val Leu  
 1 5 10 15  
 Leu Leu Leu Leu Leu Leu Pro Pro Leu Leu Leu Ala Gly Ala Val  
 20 25 30  
 Pro Pro Gly Arg Gly Arg Ala Ala Gly Pro Gln Glu Asp Val Asp Glu  
 35 40 45  
 Cys Ala Gln Gly Leu Asp Asp Cys His Ala Asp Ala Leu Cys Gln Asn  
 50 55 60  
 Thr Pro Thr Ser Tyr Lys Cys Ser Cys Lys Pro Gly Tyr Gln Gly Glu  
 65 70 75 80  
 Gly Arg Gln Cys Glu Asp Ile Asp Glu Cys Gly Asn Glu Leu Asn Gly  
 85 90 95  
 Gly Cys Val His Asp Cys Leu Asn Ile Pro Gly Asn Tyr Arg Cys Thr  
 100 105 110  
 Cys Phe Asp Gly Phe Met Leu Ala His Asp Gly His Asn Cys Leu Asp  
 115 120 125  
 Val Asp Glu Cys Leu Glu Asn Asn Gly Gly Cys Gln His Thr Cys Val  
 130 135 140  
 Asn Val Met Gly Ser Tyr Glu Cys Cys Cys Lys Glu Gly Phe Phe Leu  
 145 150 155 160  
 Ser Asp Asn Gln His Thr Cys Ile His Arg Ser Glu Glu Gly Leu Ser  
 165 170 175  
 Cys Met Asn Lys Asp His Gly Cys Ser His Ile Cys Lys Glu Ala Pro  
 180 185 190  
 Arg Gly Ser Val Ala Cys Glu Cys Arg Pro Gly Phe Glu Leu Ala Lys  
 195 200 205  
 Asn Gln Arg Asp Cys Ile Leu Thr Cys Asn His Gly Asn Gly Gly Cys  
 210 215 220  
 Gln His Ser Cys Asp Asp Thr Ala Asp Gly Pro Glu Cys Ser Cys His  
 225 230 235 240  
 Pro Gln Tyr Lys Met His Thr Asp Gly Arg Ser Cys Leu Glu Arg Glu  
 245 250 255  
 Asp Thr Val Leu Glu Val Thr Glu Ser Asn Thr Thr Ser Val Val Asp  
 260 265 270  
 Gly Asp Lys Arg Val Lys Arg Arg Leu Leu Met Glu Thr Cys Ala Val  
 275 280 285  
 Asn Asn Gly Gly Cys Asp Arg Thr Cys Lys Asp Thr Ser Thr Gly Val  
 290 295 300  
 His Cys Ser Cys Pro Val Gly Phe Thr Leu Gln Leu Asp Gly Lys Thr  
 305 310 315 320  
 Cys Lys Asp Ile Asp Glu Cys Gln Thr Arg Asn Gly Gly Cys Asp His  
 325 330 335  
 Phe Cys Lys Asn Ile Val Gly Ser Phe Asp Cys Gly Cys Lys Lys Gly  
 340 345 350  
 Phe Lys Leu Leu Thr Asp Glu Lys Ser Cys Gln Asp Val Asp Glu Cys  
 355 360 365  
 Ser Leu Asp Arg Thr Cys Asp His Ser Cys Ile Asn His Pro Gly Thr  
 370 375 380  
 Phe Ala Cys Ala Cys Asn Arg Gly Tyr Thr Leu Tyr Gly Phe Thr His  
 385 390 395 400  
 Cys Gly Asp Thr Asn Glu Cys Ser Ile Asn Asn Gly Gly Cys Gln Gln  
 405 410 415  
 Val Cys Val Asn Thr Val Gly Ser Tyr Glu Cys Gln Cys His Pro Gly  
 420 425 430  
 Tyr Lys Leu His Trp Asn Lys Lys Asp Cys Val Glu Val Lys Gly Leu  
 435 440 445  
 Leu Pro Thr Ser Val Ser Pro Arg Val Ser Leu His Cys Gly Lys Ser  
 450 455 460  
 Gly Gly Gly Asp Gly Cys Phe Leu Arg Cys His Ser Gly Ile His Leu  
 465 470 475 480

Ser	Ser	Asp	Val	Thr	Thr	Ile	Arg	Thr	Ser	Val	Thr	Phe	Lys	Leu	Asn	
				485					490					495		
Glu	Gly	Lys	Cys	Ser	Leu	Lys	Asn	Ala	Glu	Leu	Phe	Pro	Glu	Gly	Leu	
			500					505					510			
Arg	Pro	Ala	Leu	Pro	Glu	Lys	His	Ser	Ser	Val	Lys	Glu	Ser	Phe	Arg	
		515					520					525				
Tyr	Val	Asn	Leu	Thr	Cys	Ser	Ser	Gly	Lys	Gln	Val	Pro	Gly	Ala	Pro	
	530					535					540					
Gly	Arg	Pro	Ser	Thr	Pro	Lys	Glu	Met	Phe	Ile	Thr	Val	Glu	Phe	Glu	
545					550					555					560	
Leu	Glu	Thr	Asn	Gln	Lys	Glu	Val	Thr	Ala	Ser	Cys	Asp	Leu	Ser	Cys	
			565						570						575	
Ile	Val	Lys	Arg	Thr	Glu	Lys	Arg	Leu	Arg	Lys	Ala	Ile	Arg	Thr	Leu	
			580					585						590		
Arg	Lys	Ala	Val	His	Arg	Glu	Gln	Phe	His	Leu	Gln	Leu	Ser	Gly	Met	
		595					600					605				
Asn	Leu	Asp	Val	Ala	Lys	Lys	Pro	Pro	Arg	Thr	Ser	Glu	Arg	Gln	Ala	
	610					615					620					
Glu	Ser	Cys	Gly	Val	Gly	Gln	Gly	His	Ala	Glu	Asn	Gln	Cys	Val	Ser	
625					630					635					640	
Cys	Arg	Ala	Gly	Thr	Tyr	Tyr	Asp	Gly	Ala	Arg	Glu	Arg	Cys	Ile	Leu	
			645						650					655		
Cys	Pro	Asn	Gly	Thr	Phe	Gln	Asn	Glu	Glu	Gly	Gln	Met	Thr	Cys	Glu	
			660					665						670		
Pro	Cys	Pro	Arg	Pro	Gly	Asn	Ser	Gly	Ala	Leu	Lys	Thr	Pro	Glu	Ala	
		675				680						685				
Trp	Asn	Met	Ser	Glu	Cys	Gly	Gly	Leu	Cys	Gln	Pro	Gly	Glu	Tyr	Ser	
	690					695					700					
Ala	Asp	Gly	Phe	Ala	Pro	Cys	Gln	Leu	Cys	Ala	Leu	Gly	Thr	Phe	Gln	
705					710					715					720	
Pro	Glu	Ala	Gly	Arg	Thr	Ser	Cys	Phe	Pro	Cys	Gly	Gly	Gly	Leu	Ala	
			725						730					735		
Thr	Lys	His	Gln	Gly	Ala	Thr	Ser	Phe	Gln	Asp	Cys	Glu	Thr	Arg	Val	
			740					745						750		
Gln	Cys	Ser	Pro	Gly	His	Phe	Tyr	Asn	Thr	Thr	Thr	His	Arg	Cys	Ile	
		755					760					765				
Arg	Cys	Pro	Val	Gly	Thr	Tyr	Gln	Pro	Glu	Phe	Gly	Lys	Asn	Asn	Cys	
		770				775						780				
Val	Ser	Cys	Pro	Gly	Asn	Thr	Thr	Thr	Asp	Phe	Asp	Gly	Ser	Thr	Asn	
785					790					795					800	
Ile	Thr	Gln	Cys	Lys	Asn	Arg	Arg	Cys	Gly	Gly	Glu	Leu	Gly	Asp	Phe	
			805						810					815		
Thr	Gly	Tyr	Ile	Glu	Ser	Pro	Asn	Tyr	Pro	Gly	Asn	Tyr	Pro	Ala	Asn	
			820					825						830		
Thr	Glu	Cys	Thr	Trp	Thr	Ile	Asn	Pro	Pro	Pro	Lys	Arg	Arg	Ile	Leu	
		835					840					845				
Ile	Val	Val	Pro	Glu	Ile	Phe	Leu	Pro	Ile	Glu	Asp	Asp	Cys	Gly	Asp	
	850					855					860					
Tyr	Leu	Val	Met	Arg	Lys	Thr	Ser	Ser	Ser	Asn	Ser	Val	Thr	Thr	Tyr	
865					870					875					880	
Glu	Thr	Cys	Gln	Thr	Tyr	Glu	Arg	Pro	Ile	Ala	Phe	Thr	Ser	Arg	Ser	
			885						890					895		
Lys	Lys	Leu	Trp	Ile	Gln	Phe	Lys	Ser	Asn	Glu	Gly	Asn	Ser	Ala	Arg	
			900					905						910		
Gly	Phe	Gln	Val	Pro	Tyr	Val	Thr	Tyr	Asp	Glu	Asp	Tyr	Gln	Glu	Leu	
		915					920					925				
Ile	Glu	Asp	Ile	Val	Arg	Asp	Gly	Arg	Leu	Tyr	Ala	Ser	Glu	Asn	His	
	930					935					940					
Gln	Glu	Ile	Leu	Lys	Asp	Lys	Lys	Leu	Ile	Lys	Ala	Leu	Phe	Asp	Val	
945					950					955					960	
Leu	Ala	His	Pro	Gln	Asn	Tyr	Phe	Lys	Tyr	Thr	Ala	Gln	Glu	Ser	Arg	
				965					970						975	



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Glu Met Phe Pro Arg Ser Phe Ile Arg Leu Leu Arg Ser Lys Val Ser  
 980 985 990  
 Arg Phe Leu Arg Pro Tyr Lys  
 995

&lt;210&gt; 301

&lt;211&gt; 340

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 301

Met Cys Ala Gln Tyr Cys Ile Ser Phe Ala Asp Val Glu Lys Ala His  
 1 5 10 15  
 Ile Asn Ile Arg Asp Ser Ile His Leu Thr Pro Val Leu Thr Ser Ser  
 20 25 30  
 Ile Leu Asn Gln Leu Thr Gly Arg Asn Leu Phe Phe Lys Cys Glu Leu  
 35 40 45  
 Phe Gln Lys Thr Gly Ser Phe Lys Ile Arg Gly Ala Leu Asn Ala Val  
 50 55 60  
 Arg Ser Leu Val Pro Asp Ala Leu Glu Arg Lys Pro Lys Ala Val Val  
 65 70 75 80  
 Thr His Ser Ser Gly Asn His Gly Gln Ala Leu Thr Tyr Ala Ala Lys  
 85 90 95  
 Leu Glu Gly Ile Pro Ala Tyr Ile Val Val Pro Gln Thr Ala Pro Asp  
 100 105 110  
 Cys Lys Lys Leu Ala Ile Gln Ala Tyr Gly Ala Ser Ile Val Tyr Cys  
 115 120 125  
 Glu Pro Ser Asp Glu Ser Arg Glu Asn Val Ala Lys Arg Val Thr Glu  
 130 135 140  
 Glu Thr Glu Gly Ile Met Val His Pro Asn Gln Glu Pro Ala Val Ile  
 145 150 155 160  
 Ala Gly Gln Gly Thr Ile Ala Leu Glu Val Leu Asn Gln Val Pro Leu  
 165 170 175  
 Val Asp Ala Leu Val Val Pro Val Gly Gly Gly Met Leu Ala Gly  
 180 185 190  
 Ile Ala Ile Thr Val Lys Ala Leu Lys Pro Ser Val Lys Val Tyr Ala  
 195 200 205  
 Ala Glu Pro Ser Asn Ala Asp Asp Cys Tyr Gln Ser Lys Leu Lys Gly  
 210 215 220  
 Lys Leu Met Pro Asn Leu Tyr Pro Pro Glu Thr Ile Ala Asp Gly Val  
 225 230 235 240  
 Lys Ser Ser Ile Gly Leu Asn Thr Trp Pro Ile Ile Arg Asp Leu Val  
 245 250 255  
 Asp Asp Ile Phe Thr Val Thr Glu Asp Glu Ile Lys Cys Ala Thr Gln  
 260 265 270  
 Leu Val Trp Glu Arg Met Lys Leu Ile Glu Pro Thr Ala Gly Val  
 275 280 285  
 Gly Val Ala Ala Val Leu Ser Gln His Phe Gln Thr Val Ser Pro Glu  
 290 295 300  
 Val Lys Asn Ile Cys Ile Val Leu Ser Gly Gly Asn Val Asp Leu Thr  
 305 310 315 320  
 Ser Ser Ile Thr Trp Val Lys Gln Ala Glu Arg Pro Ala Ser Tyr Gln  
 325 330 335  
 Ser Val Ser Val  
 340

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&lt;210&gt; 302

&lt;211&gt; 218

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 302

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Met Asn Arg Leu Phe Gly Lys Ala Lys Pro Lys Ala Pro Arg Pro Ser
1      5      10      15
Leu Thr Asp Cys Ile Gly Thr Val Asp Ser Arg Ala Glu Ser Ile Asp
20      25      30
Lys Lys Ile Ser Arg Leu Asp Ala Glu Leu Val Lys Tyr Lys Asp Gln
35      40      45
Ile Lys Lys Met Arg Glu Gly Pro Ala Lys Asn Met Val Lys Gln Lys
50      55      60
Ala Leu Arg Val Leu Lys Gln Lys Arg Met Tyr Glu Gln Gln Arg Asp
65      70      75      80
Asn Leu Ala Asn Ser His Ser Thr Trp Thr Gly His Tyr Thr Ile Gln
85      90      95
Ser Leu Lys Asp Thr Lys Thr Thr Val Asp Ala Met Lys Leu Gly Val
100      105      110
Lys Glu Met Lys Lys Ala Tyr Lys Pro Val Lys Ile Asp Gln Ile Glu
115      120      125
Asp Leu Gln Asp Gln Leu Glu Asp Met Met Glu Asp Ala Asn Glu Ile
130      135      140
Gln Glu Ala Leu Ser Arg Ser Tyr Gly Thr Pro Glu Leu Asp Glu Asp
145      150      155      160
Asp Leu Glu Ala Glu Leu Asp Ala Leu Gly Asp Glu Leu Leu Ala Asp
165      170      175
Glu Asp Ser Ser Tyr Leu Asp Glu Ala Ala Ser Ala Pro Ala Ile Pro
180      185      190
Glu Gly Val Pro Thr Asp Thr Lys Asn Lys Asp Gly Val Leu Val Asp
195      200      205
Glu Phe Gly Leu Pro Gln Ile Pro Ala Ser
210      215

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&lt;210&gt; 303

&lt;211&gt; 635

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 303

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Met Ala Pro Pro Leu Leu Leu Leu Leu Leu Ala Ser Gly Ala Ala Ala
1      5      10      15
Cys Pro Leu Pro Cys Val Cys Gln Asn Leu Ser Glu Ser Leu Ser Thr
20      25      30
Leu Cys Ala His Arg Gly Leu Leu Phe Val Pro Pro Asn Val Asp Arg
35      40      45
Arg Thr Val Glu Leu Arg Leu Ala Asp Asn Phe Ile Gln Ala Leu Gly
50      55      60
Pro Pro Asp Phe Arg Asn Met Thr Gly Leu Val Asp Leu Thr Leu Ser
65      70      75      80

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Arg Asn Ala Ile Thr Arg Ile Gly Ala Arg Ala Phe Gly Asp Leu Glu  
 85 90 95  
 Ser Leu Arg Ser Leu His Leu Asp Gly Asn Arg Leu Val Glu Leu Gly  
 100 105 110  
 Thr Gly Ser Leu Arg Gly Pro Val Asn Leu Gln His Leu Ile Leu Ser  
 115 120 125  
 Gly Asn Gln Leu Gly Arg Ile Ala Pro Gly Ala Phe Asp Asp Phe Leu  
 130 135 140  
 Glu Ser Leu Glu Asp Leu Asp Leu Ser Tyr Asn Asn Leu Arg Gln Val  
 145 150 155 160  
 Pro Trp Ala Gly Ile Gly Ala Met Pro Ala Leu His Thr Leu Asn Leu  
 165 170 175  
 Asp His Asn Leu Ile Asp Ala Leu Pro Pro Gly Ala Phe Ala Gln Leu  
 180 185 190  
 Gly Gln Leu Ser Arg Leu Asp Leu Thr Ser Asn Arg Leu Ala Thr Leu  
 195 200 205  
 Ala Pro Asp Pro Leu Phe Ser Arg Gly Arg Asp Ala Glu Ala Ser Pro  
 210 215 220  
 Ala Pro Leu Val Leu Ser Phe Ser Gly Asn Pro Leu His Cys Asn Cys  
 225 230 235 240  
 Glu Leu Leu Trp Leu Arg Arg Leu Ala Arg Pro Asp Asp Leu Glu Thr  
 245 250 255  
 Cys Ala Ser Pro Pro Gly Leu Ala Gly Arg Tyr Phe Trp Ala Val Pro  
 260 265 270  
 Glu Gly Glu Phe Ser Cys Glu Pro Pro Leu Ile Ala Arg His Thr Gln  
 275 280 285  
 Arg Leu Trp Val Leu Glu Gly Gln Arg Ala Thr Leu Arg Cys Arg Ala  
 290 295 300  
 Leu Gly Asp Pro Ala Pro Thr Met His Trp Val Gly Pro Asp Asp Arg  
 305 310 315 320  
 Leu Val Gly Asn Ser Ser Arg Ala Arg Ala Phe Pro Asn Gly Thr Leu  
 325 330 335  
 Glu Ile Gly Val Thr Gly Ala Gly Asp Ala Gly Gly Tyr Thr Cys Ile  
 340 345 350  
 Ala Thr Asn Pro Ala Gly Glu Ala Thr Ala Arg Val Glu Leu Arg Val  
 355 360 365  
 Leu Ala Leu Pro His Gly Gly Asn Ser Ser Ala Glu Gly Gly Arg Pro  
 370 375 380  
 Gly Pro Ser Asp Ile Ala Ser Ala Arg Thr Ala Ala Glu Gly Glu  
 385 390 395 400  
 Gly Thr Leu Glu Ser Glu Pro Ala Val Gln Val Thr Glu Val Thr Ala  
 405 410 415  
 Thr Ser Gly Leu Val Ser Trp Gly Pro Gly Arg Pro Ala Asp Pro Val  
 420 425 430  
 Trp Met Phe Gln Ile Gln Tyr Asn Ser Ser Glu Asp Glu Thr Leu Ile  
 435 440 445  
 Tyr Arg Ile Val Pro Ala Ser Ser His His Phe Leu Leu Lys His Leu  
 450 455 460  
 Val Pro Gly Ala Asp Tyr Asp Leu Cys Leu Leu Ala Leu Ser Pro Ala  
 465 470 475 480  
 Ala Gly Pro Ser Asp Leu Thr Ala Thr Arg Leu Leu Gly Cys Ala His  
 485 490 495  
 Phe Ser Thr Leu Pro Ala Ser Pro Leu Cys His Ala Leu Gln Ala His  
 500 505 510  
 Val Leu Gly Thr Leu Thr Val Ala Val Gly Gly Val Leu Val Ala  
 515 520 525  
 Ala Leu Leu Val Phe Thr Val Ala Leu Leu Val Arg Gly Arg Gly Ala  
 530 535 540  
 Gly Asn Gly Arg Leu Pro Leu Lys Leu Ser His Val Gln Ser Gln Thr  
 545 550 555 560  
 Asn Gly Gly Pro Ser Pro Thr Pro Lys Ala His Pro Pro Arg Ser Pro  
 565 570 575

Pro	Pro	Arg	Pro	Gln	Arg	Ser	Cys	Ser	Leu	Asp	Leu	Gly	Asp	Ala	Gly
			580					585					590		
Cys	Tyr	Gly	Tyr	Ala	Arg	Arg	Leu	Gly	Gly	Ala	Trp	Ala	Arg	Arg	Ser
		595					600					605			
His	Ser	Val	His	Gly	Gly	Leu	Leu	Gly	Ala	Gly	Cys	Arg	Gly	Val	Gly
	610					615					620				
Gly	Ser	Ala	Glu	Arg	Leu	Glu	Glu	Ser	Val	Val					
625					630					635					

**<210> 304**

**<211> 498**

<212> PRT

<213> Homo sapiens

**<400> 304**

Met	Asp	Val	Thr	Asp	His	Tyr	Glu	Asp	Val	Arg	Lys	Ile	Tyr	Asp	Asp
1				5					10					15	
Phe	Leu	Lys	Asn	Ser	Asn	Met	Leu	Asp	Leu	Ile	Asp	Val	Tyr	Gln	Lys
			20					25					30		
Cys	Arg	Ala	Leu	Thr	Ser	Asn	Cys	Glu	Asn	Tyr	Asn	Thr	Val	Ser	Pro
		35					40					45			
Ser	Gln	Leu	Leu	Asp	Phe	Leu	Ser	Gly	Lys	Gln	Tyr	Ala	Val	Gly	Asp
	50					55					60				
Glu	Thr	Asp	Leu	Ser	Ile	Pro	Thr	Ser	Pro	Thr	Ser	Lys	Tyr	Asn	Arg
65				70					75					80	
Asp	Asn	Glu	Lys	Val	Gln	Leu	Leu	Ala	Arg	Lys	Ile	Ile	Phe	Ser	Tyr
				85				90						95	
Leu	Asn	Leu	Leu	Val	Asn	Ser	Lys	Asn	Asp	Leu	Ala	Val	Ala	Tyr	Ile
			100					105					110		
Leu	Asn	Ile	Pro	Asp	Arg	Gly	Leu	Gly	Arg	Glu	Ala	Phe	Thr	Asp	Leu
		115				120					125				
Lys	His	Ala	Ala	Arg	Glu	Lys	Gln	Met	Ser	Ile	Phe	Leu	Val	Ala	Thr
	130					135					140				
Ser	Phe	Ile	Arg	Thr	Ile	Glu	Leu	Gly	Gly	Lys	Gly	Tyr	Ala	Pro	Pro
145				150					155						
Pro	Ser	Asp	Pro	Leu	Arg	Thr	His	Val	Lys	Gly	Leu	Ser	Asn	Phe	Ile
				165				170					175		
Asn	Phe	Ile	Asp	Lys	Leu	Asp	Glu	Ile	Leu	Gly	Glu	Ile	Pro	Asn	Pro
			180				185						190		
Ser	Ile	Ala	Gly	Gly	Gln	Ile	Leu	Ser	Val	Ile	Lys	Met	Gln	Leu	Ile
		195				200						205			
Lys	Gly	Gln	Asn	Ser	Arg	Asp	Pro	Phe	Cys	Lys	Ala	Ile	Glu	Glu	Val
	210					215					220				
Ala	Gln	Asp	Leu	Asp	Leu	Arg	Ile	Lys	Asn	Ile	Asn	Ser	Gln	Glu	
225				230					235						
Gly	Val	Val	Ala	Leu	Ser	Thr	Thr	Asp	Ile	Ser	Pro	Ala	Arg	Pro	Lys
				245				250					255		
Ser	His	Ala	Ile	Asn	His	Gly	Thr	Ala	Tyr	Cys	Gly	Arg	Asp	Thr	Val
			260				265						270		
Lys	Ala	Leu	Leu	Val	Leu	Leu	Asp	Glu	Glu	Ala	Ala	Asn	Ala	Pro	Thr
		275					280					285			
Lys	Asn	Lys	Ala	Glu	Leu	Leu	Tyr	Asp	Glu	Glu	Asp	Thr	Ile	His	His
	290					295					300				
His	Gly	Thr	Ser	Ile	Leu	Thr	Leu	Phe	Arg	Ser	Pro	Thr	Gln	Val	Asn
305				310					315						
Asn	Leu	Ile	Lys	Pro	Leu	Arg	Glu	Arg	Ile	Cys	Val	Ser	Met	Gln	Glu
				325					330					335	

Lys Lys Ile Lys Met Lys Gln Thr Leu Ile Arg Ser Gln Phe Ala Cys  
 340 345 350  
 Thr Tyr Lys Asp Asp Tyr Met Ile Ser Lys Asp Asn Trp Asn Asn Val  
 355 360 365  
 Asn Leu Ala Ser Lys Pro Leu Cys Val Leu Tyr Met Glu Asn Asp Leu  
 370 375 380  
 Ser Glu Gly Val Asn Pro Ser Val Gly Arg Ser Thr Ile Gly Thr Ser  
 385 390 395 400  
 Phe Gly Asn Val His Leu Asp Arg Ser Lys Asn Glu Lys Val Ser Arg  
 405 410 415  
 Lys Ser Thr Ser Gln Thr Gly Asn Lys Ser Ser Lys Arg Lys Gln Val  
 420 425 430  
 Asp Leu Asp Gly Glu Asn Ile Leu Cys Asp Asn Arg Asn Glu Pro Pro  
 435 440 445  
 Gln His Lys Asn Ala Lys Ile Pro Lys Lys Ser Asn Asp Ser Gln Asn  
 450 455 460  
 Arg Leu Tyr Gly Lys Leu Ala Lys Val Ala Lys Ser Asn Lys Cys Thr  
 465 470 475 480  
 Ala Lys Asp Lys Leu Ile Ser Gly Gln Ala Lys Leu Thr Gln Phe Phe  
 485 490 495  
 Arg Leu

&lt;210&gt; 305

&lt;211&gt; 172

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 305

Met Arg Asp Ile Ala Ile Leu Lys Glu Lys Gln Glu Lys Glu Ile Gln  
 1 5 10 15  
 Thr Leu Gln Glu Glu Thr Lys Lys Val Gln Ala Glu Thr Ala Ser Lys  
 20 25 30  
 Thr Arg Glu Val Gln Ala Gln Leu Leu Gln Glu Lys Arg Leu Leu Glu  
 35 40 45  
 Lys Gln Leu Ser Glu Pro Asp Arg Arg Leu Leu Gly Lys Arg Lys Arg  
 50 55 60  
 Arg Glu Leu Asn Met Lys Ala Gln Ala Leu Lys Leu Ala Ala Lys Arg  
 65 70 75 80  
 Phe Ile Phe Glu Tyr Ser Cys Gly Ile Asn Arg Glu Asn Gln Gln Phe  
 85 90 95  
 Lys Lys Glu Leu Leu Gln Leu Ile Glu Gln Ala Gln Lys Leu Thr Ala  
 100 105 110  
 Thr Gln Ser His Leu Glu Asn Arg Lys Gln Gln Leu Gln Gln Glu Gln  
 115 120 125  
 Trp Tyr Leu Glu Ser Leu Ile Gln Ala Arg Gln Arg Leu Gln Gly Ser  
 130 135 140  
 His Asn Gln Cys Leu Asn Arg Gln Asp Val Pro Lys Thr Thr Pro Ser  
 145 150 155 160  
 Leu Pro Gln Gly Thr Lys Ser Arg Ile Asn Pro Lys  
 165 170

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&lt;210&gt; 306

&lt;211&gt; 330

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 306

Met Arg Arg Pro Ser Val Arg Ala Ala Gly Leu Val Leu Cys Thr Leu  
 1 5 10 15  
 Cys Tyr Leu Leu Val Gly Ala Ala Val Phe Asp Ala Leu Glu Ser Glu  
 20 25 30  
 Ala Glu Ser Gly Arg Gln Arg Leu Val Gln Lys Arg Gly Ala Leu  
 35 40 45  
 Arg Arg Lys Phe Gly Phe Ser Ala Glu Asp Tyr Arg Glu Leu Glu Arg  
 50 55 60  
 Leu Ala Leu Gln Ala Glu Pro His Arg Ala Gly Arg Gln Trp Lys Phe  
 65 70 75 80  
 Pro Gly Ser Phe Tyr Phe Ala Ile Thr Val Ile Thr Thr Ile Gly Tyr  
 85 90 95  
 Gly His Ala Ala Pro Gly Thr Asp Ser Gly Lys Val Phe Cys Met Phe  
 100 105 110  
 Tyr Ala Leu Leu Gly Ile Pro Leu Thr Leu Val Thr Phe Gln Ser Leu  
 115 120 125  
 Gly Glu Arg Leu Asn Ala Val Arg Arg Leu Leu Leu Ala Ala Lys  
 130 135 140  
 Cys Cys Leu Gly Leu Arg Trp Thr Cys Val Ser Thr Glu Asn Leu Val  
 145 150 155 160  
 Val Ala Gly Leu Leu Ala Cys Ala Ala Thr Leu Ala Leu Gly Ala Val  
 165 170 175  
 Ala Phe Ser His Phe Glu Gly Trp Thr Phe Phe His Ala Tyr Tyr Tyr  
 180 185 190  
 Cys Phe Ile Thr Leu Thr Thr Ile Gly Phe Gly Asp Phe Val Ala Leu  
 195 200 205  
 Gln Ser Gly Glu Ala Leu Gln Arg Lys Leu Pro Tyr Val Ala Phe Ser  
 210 215 220  
 Phe Leu Tyr Ile Leu Leu Gly Leu Thr Val Ile Gly Ala Phe Leu Asn  
 225 230 235 240  
 Leu Val Val Leu Arg Phe Leu Val Ala Ser Ala Asp Trp Pro Glu Arg  
 245 250 255  
 Ala Ala Arg Pro Pro Ser Pro Arg Pro Pro Gly Ala Pro Glu Ser Arg  
 260 265 270  
 Gly Leu Trp Leu Pro Arg Arg Pro Ala Arg Ser Val Gly Ser Ala Ser  
 275 280 285  
 Val Phe Cys His Val His Lys Leu Glu Arg Cys Ala Arg Asp Asn Leu  
 290 295 300  
 Gly Phe Ser Pro Pro Ser Ser Pro Gly Val Val Arg Gly Gly Gln Ala  
 305 310 315 320  
 Pro Arg Pro Gly Ala Arg Trp Lys Ser Ile  
 325 330

&lt;210&gt; 307

&lt;211&gt; 741

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 307  
 Met Glu Ser Arg Asp His Asn Asn Pro Gln Glu Gly Pro Thr Ser Ser  
 1 5 10 15  
 Ser Gly Arg Arg Ala Ala Val Glu Asp Asn His Leu Leu Ile Lys Ala  
 20 25 30  
 Val Gln Asn Glu Asp Val Asp Leu Val Gln Gln Leu Leu Glu Gly Gly  
 35 40 45  
 Ala Asn Val Asn Phe Gln Glu Glu Gly Gly Trp Thr Pro Leu His  
 50 55 60  
 Asn Ala Val Gln Met Ser Arg Glu Asp Ile Val Glu Leu Leu Leu Arg  
 65 70 75 80  
 His Gly Ala Asp Pro Val Leu Arg Lys Lys Asn Gly Ala Thr Pro Phe  
 85 90 95  
 Ile Leu Ala Ala Ile Ala Gly Ser Val Lys Leu Leu Lys Leu Phe Leu  
 100 105 110  
 Ser Lys Gly Ala Asp Val Asn Glu Cys Asp Phe Tyr Gly Phe Thr Ala  
 115 120 125  
 Phe Met Glu Ala Ala Val Tyr Gly Lys Val Lys Ala Leu Lys Phe Leu  
 130 135 140  
 Tyr Lys Arg Gly Ala Asn Val Asn Leu Arg Arg Lys Thr Lys Glu Asp  
 145 150 155 160  
 Gln Glu Arg Leu Arg Lys Gly Gly Ala Thr Ala Leu Met Asp Ala Ala  
 165 170 175  
 Glu Lys Gly His Val Glu Val Leu Lys Ile Leu Leu Asp Glu Met Gly  
 180 185 190  
 Ala Asp Val Asn Ala Cys Asp Asn Met Gly Arg Asn Ala Leu Ile His  
 195 200 205  
 Ala Leu Leu Ser Ser Asp Asp Ser Asp Val Glu Ala Ile Thr His Leu  
 210 215 220  
 Leu Leu Asp His Gly Ala Asp Val Asn Val Arg Gly Glu Arg Gly Lys  
 225 230 235 240  
 Thr Pro Leu Ile Leu Ala Val Glu Lys Lys His Leu Gly Leu Val Gln  
 245 250 255  
 Arg Leu Leu Glu Gln Glu His Ile Glu Ile Asn Asp Thr Asp Ser Asp  
 260 265 270  
 Gly Lys Thr Ala Leu Leu Leu Ala Val Glu Leu Lys Leu Lys Lys Ile  
 275 280 285  
 Ala Glu Leu Leu Cys Lys Arg Gly Ala Ser Thr Asp Cys Gly Asp Leu  
 290 295 300  
 Val Met Thr Ala Arg Arg Asn Tyr Asp His Ser Leu Val Lys Val Leu  
 305 310 315 320  
 Leu Ser His Gly Ala Lys Glu Asp Phe His Pro Pro Ala Glu Asp Trp  
 325 330 335  
 Lys Pro Gln Ser Ser His Trp Gly Ala Ala Leu Lys Asp Leu His Arg  
 340 345 350  
 Ile Tyr Arg Pro Met Ile Gly Lys Leu Lys Phe Phe Ile Asp Glu Lys  
 355 360 365  
 Tyr Lys Ile Ala Asp Thr Ser Glu Gly Gly Ile Tyr Leu Gly Phe Tyr  
 370 375 380  
 Glu Lys Gln Glu Val Ala Val Lys Thr Phe Cys Glu Gly Ser Pro Arg  
 385 390 395 400  
 Ala Gln Arg Glu Val Ser Cys Leu Gln Ser Ser Arg Glu Asn Ser His  
 405 410 415  
 Leu Val Thr Phe Tyr Gly Ser Glu Ser His Arg Gly His Leu Phe Val  
 420 425 430  
 Cys Val Thr Leu Cys Glu Gln Thr Leu Glu Ala Cys Leu Asp Val His  
 435 440 445  
 Arg Gly Glu Asp Val Glu Asn Glu Glu Asp Glu Phe Ala Arg Asn Val  
 450 455 460

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Leu Ser Ser Ile Phe Lys Ala Val Gln Glu Leu His Leu Ser Cys Gly  
 465 470 475 480  
 Tyr Thr His Gln Asp Leu Gln Pro Gln Asn Ile Leu Ile Asp Ser Lys  
 485 490 495  
 Lys Ala Ala His Leu Ala Asp Phe Asp Lys Ser Ile Lys Trp Ala Gly  
 500 505 510  
 Asp Pro Gln Glu Val Lys Arg Asp Leu Glu Asp Leu Gly Arg Leu Val  
 515 520 525  
 Leu Tyr Val Val Lys Lys Gly Ser Ile Ser Phe Glu Asp Leu Lys Ala  
 530 535 540  
 Gln Ser Asn Glu Glu Val Val Gln Leu Ser Pro Asp Glu Glu Thr Lys  
 545 550 555 560  
 Asp Leu Ile His Arg Leu Phe His Pro Gly Glu His Val Arg Asp Cys  
 565 570 575  
 Leu Ser Asp Leu Glu Gly His Pro Phe Trp Thr Trp Glu Ser Arg  
 580 585 590  
 Tyr Arg Thr Leu Arg Asn Val Gly Asn Glu Ser Asp Ile Lys Thr Arg  
 595 600 605  
 Lys Ser Glu Ser Glu Ile Leu Arg Leu Leu Gln Pro Gly Pro Ser Glu  
 610 615 620  
 His Ser Lys Ser Phe Asp Lys Trp Thr Thr Lys Ile Asn Glu Cys Val  
 625 630 635 640  
 Met Lys Lys Met Asn Lys Phe Tyr Glu Lys Arg Gly Asn Phe Tyr Gln  
 645 650 655  
 Asn Thr Val Gly Asp Leu Leu Lys Phe Ile Arg Asn Leu Gly Glu His  
 660 665 670  
 Ile Asp Glu Glu Lys His Lys Lys Met Lys Leu Lys Ile Gly Asp Pro  
 675 680 685  
 Ser Leu Tyr Phe Gln Lys Thr Phe Pro Asp Leu Val Ile Tyr Val Tyr  
 690 695 700  
 Thr Lys Leu Gln Asn Thr Glu Tyr Arg Lys His Phe Pro Gln Thr His  
 705 710 715 720  
 Ser Pro Asn Lys Pro Gln Cys Asp Gly Ala Gly Gly Ala Ser Gly Leu  
 725 730 735  
 Ala Ser Pro Gly Cys  
 740

&lt;210&gt; 308

&lt;211&gt; 651

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 308

Met Ser Gly Val Arg Ala Val Arg Ile Ser Ile Glu Ser Ala Cys Glu  
 1 5 10 15  
 Lys Gln Val His Glu Val Gly Leu Asp Gly Thr Glu Thr Tyr Leu Pro  
 20 25 30  
 Pro Leu Ser Met Ser Gln Asn Leu Ala Arg Leu Ala Gln Arg Ile Asp  
 35 40 45  
 Phe Ser Gln Gly Ser Gly Ser Glu Glu Glu Ala Ala Gly Thr Glu  
 50 55 60  
 Gly Asp Ala Gln Glu Trp Pro Gly Ala Gly Ser Ser Ala Asp Gln Asp  
 65 70 75 80  
 Asp Glu Glu Gly Val Val Lys Phe Gln Pro Ser Leu Trp Pro Trp Asp  
 85 90 95  
 Ser Val Arg Asn Leu Arg Ser Ala Leu Thr Glu Met Cys Val Leu  
 100 105 110



Tyr Asp Val Leu Ser Ile Val Arg Asp Lys Lys Phe Met Thr Leu Asp  
 115 120 125  
 Pro Val Ser Gln Asp Ala Leu Pro Pro Lys Gln Asn Pro Gln Thr Leu  
 130 135 140  
 Gln Leu Ile Ser Lys Lys Lys Ser Leu Ala Gly Ala Ala Gln Ile Leu  
 145 150 155  
 Leu Lys Gly Ala Glu Arg Leu Thr Lys Ser Val Thr Glu Asn Gln Glu  
 165 170 175  
 Asn Lys Leu Gln Arg Asp Phe Asn Ser Glu Leu Leu Arg Leu Arg Gln  
 180 185 190  
 His Trp Lys Leu Arg Lys Val Gly Asp Lys Ile Leu Gly Asp Leu Ser  
 195 200 205  
 Tyr Arg Ser Ala Gly Ser Leu Phe Pro His His Gly Thr Phe Glu Val  
 210 215 220  
 Ile Lys Asn Thr Asp Leu Asp Leu Asp Lys Lys Ile Pro Glu Asp Tyr  
 225 230 235 240  
 Cys Pro Leu Asp Val Gln Ile Pro Ser Asp Leu Glu Gly Ser Ala Tyr  
 245 250 255  
 Ile Lys Val Ser Ile Gln Lys Gln Ala Pro Asp Ile Gly Asp Leu Gly  
 260 265 270  
 Thr Val Asn Leu Phe Lys Arg Pro Leu Pro Lys Ser Lys Pro Gly Ser  
 275 280 285  
 Pro His Trp Gln Thr Lys Leu Glu Ala Ala Gln Asn Val Leu Leu Cys  
 290 295 300  
 Lys Glu Ile Phe Ala Gln Leu Ser Arg Glu Ala Val Gln Ile Lys Ser  
 305 310 315 320  
 Gln Val Pro His Ile Val Val Lys Asn Gln Ile Ile Ser Gln Pro Phe  
 325 330 335  
 Pro Ser Leu Gln Leu Ser Ile Ser Leu Cys His Ser Ser Asn Asp Lys  
 340 345 350  
 Lys Ser Gln Lys Phe Ala Thr Glu Lys Gln Cys Pro Glu Asp His Leu  
 355 360 365  
 Tyr Val Leu Glu His Asn Leu His Leu Leu Ile Arg Glu Phe His Lys  
 370 375 380  
 Gln Thr Leu Ser Ser Ile Met Met Pro His Pro Ala Ser Ala Pro Phe  
 385 390 395 400  
 Gly His Lys Arg Met Arg Leu Ser Gly Pro Gln Ala Phe Asp Lys Asn  
 405 410 415  
 Glu Ile Asn Ser Leu Gln Ser Ser Glu Gly Leu Leu Glu Lys Ile Ile  
 420 425 430  
 Lys Gln Ala Lys His Ile Phe Leu Arg Ser Arg Ala Ala Ala Thr Ile  
 435 440 445  
 Asp Ser Leu Ala Ser Arg Ile Glu Asp Pro Gln Ile Gln Ala His Trp  
 450 455 460  
 Ser Asn Ile Asn Asp Val Tyr Glu Ser Ser Val Lys Val Leu Ile Thr  
 465 470 475 480  
 Ser Gln Gly Tyr Glu Gln Ile Cys Lys Ser Ile Gln Leu Gln Leu Asn  
 485 490 495  
 Ile Gly Val Glu Gln Ile Arg Val Val His Arg Asp Gly Arg Val Ile  
 500 505 510  
 Thr Leu Ser Tyr Gln Glu Gln Glu Leu Gln Asp Phe Leu Leu Ser Gln  
 515 520 525  
 Met Ser Gln His Gln Val His Ala Val Gln Gln Leu Ala Lys Val Met  
 530 535 540  
 Gly Trp Gln Val Leu Ser Phe Ser Asn His Val Gly Leu Gly Pro Ile  
 545 550 555 560  
 Glu Ser Ile Gly Asn Ala Ser Ala Ile Thr Val Ala Ser Pro Ser Gly  
 565 570 575  
 Asp Tyr Ala Ile Ser Val Arg Asn Gly Pro Glu Ser Gly Ser Lys Ile  
 580 585 590  
 Met Val Gln Phe Pro Arg Asn Gln Cys Lys Asp Leu Pro Lys Ser Asp  
 595 600 605

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Val Leu Gln Asp Asn Lys Trp Ser His Leu Arg Gly Pro Phe Lys Glu  
 610 615 620  
 Val Gln Trp Asn Lys Met Glu Gly Arg Asn Phe Val Tyr Lys Met Glu  
 625 630 635 640  
 Leu Leu Met Ser Ala Leu Ser Pro Cys Leu Leu  
 645 650

&lt;210&gt; 309

&lt;211&gt; 1496

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 309  
 Met Met Ala Asn Trp Ala Glu Ala Arg Pro Leu Leu Ile Leu Ile Val  
 1 5 10 15  
 Leu Leu Gly Gln Phe Val Ser Ile Lys Ala Gln Glu Glu Asp Glu Asp  
 20 25 30  
 Glu Gly Tyr Gly Glu Glu Ile Ala Cys Thr Gln Asn Gly Gln Met Tyr  
 35 40 45  
 Leu Asn Arg Asp Ile Trp Lys Pro Ala Pro Cys Gln Ile Cys Val Cys  
 50 55 60  
 Asp Asn Gly Ala Ile Leu Cys Asp Lys Ile Glu Cys Gln Asp Val Leu  
 65 70 75 80  
 Asp Cys Ala Asp Pro Val Thr Pro Pro Gly Glu Cys Cys Pro Val Cys  
 85 90 95  
 Ser Gln Thr Pro Gly Gly Gly Asn Thr Asn Phe Gly Arg Gly Arg Lys  
 100 105 110  
 Gly Gln Lys Gly Glu Pro Gly Leu Val Pro Val Val Thr Gly Ile Arg  
 115 120 125  
 Gly Arg Pro Gly Pro Ala Gly Pro Pro Gly Ser Gln Gly Pro Arg Gly  
 130 135 140  
 Glu Arg Gly Pro Lys Gly Arg Pro Gly Pro Arg Gly Pro Gln Gly Ile  
 145 150 155 160  
 Asp Gly Glu Pro Gly Val Pro Gly Gln Pro Gly Ala Pro Gly Pro Pro  
 165 170 175  
 Gly His Pro Ser His Pro Gly Pro Asp Gly Leu Ser Arg Pro Phe Ser  
 180 185 190  
 Ala Gln Met Ala Gly Leu Asp Glu Lys Ser Gly Leu Gly Ser Gln Val  
 195 200 205  
 Gly Leu Met Pro Gly Ser Val Gly Pro Val Gly Pro Arg Gly Pro Gln  
 210 215 220  
 Gly Leu Gln Gly Gln Gln Gly Gly Ala Gly Pro Thr Gly Pro Pro Gly  
 225 230 235 240  
 Glu Pro Gly Asp Pro Gly Pro Met Gly Pro Ile Gly Ser Arg Gly Pro  
 245 250 255  
 Glu Gly Pro Pro Gly Lys Pro Gly Glu Asp Gly Glu Pro Gly Arg Asn  
 260 265 270  
 Gly Asn Pro Gly Glu Val Gly Phe Ala Gly Ser Pro Gly Ala Arg Gly  
 275 280 285  
 Phe Pro Gly Ala Pro Gly Leu Pro Gly Leu Lys Gly His Arg Gly His  
 290 295 300  
 Lys Gly Leu Glu Gly Pro Lys Gly Glu Val Gly Ala Pro Gly Ser Lys  
 305 310 315 320  
 Gly Glu Ala Gly Pro Thr Gly Pro Met Gly Ala Met Gly Pro Leu Gly  
 325 330 335  
 Pro Arg Gly Met Pro Gly Glu Arg Gly Arg Leu Gly Pro Gln Gly Ala  
 340 345 350

Pro Gly Gln Arg Gly Ala His Gly Met Pro Gly Lys Pro Gly Pro Met  
 355 360 365  
 Gly Pro Leu Gly Ile Pro Gly Ser Ser Gly Phe Pro Gly Asn Pro Gly  
 370 375 380  
 Met Lys Gly Glu Ala Gly Pro Thr Gly Ala Arg Gly Pro Glu Gly Pro  
 385 390 395 400  
 Gln Gly Gln Arg Gly Glu Thr Gly Pro Pro Gly Pro Val Gly Ser Pro  
 405 410 415  
 Gly Leu Pro Gly Ala Ile Gly Thr Asp Gly Thr Pro Gly Pro Lys Gly  
 420 425 430  
 Pro Thr Gly Ser Pro Gly Thr Ser Gly Pro Pro Gly Ser Ala Gly Pro  
 435 440 445  
 Pro Gly Ser Pro Gly Pro Gln Gly Ser Thr Gly Pro Gln Gly Asn Ser  
 450 455 460  
 Gly Leu Pro Gly Asp Pro Gly Phe Lys Gly Glu Ala Gly Pro Lys Gly  
 465 470 475 480  
 Glu Pro Gly Pro His Gly Ile Gln Gly Pro Ile Gly Pro Pro Gly Glu  
 485 490 495  
 Glu Gly Lys Arg Gly Pro Arg Gly Asp Pro Gly Thr Leu Gly Pro Pro  
 500 505 510  
 Gly Pro Val Gly Glu Arg Gly Ala Pro Gly Asn Arg Gly Phe Pro Gly  
 515 520 525  
 Ser Asp Gly Leu Pro Gly Pro Lys Gly Ala Gln Gly Glu Arg Gly Pro  
 530 535 540  
 Val Gly Ser Ser Gly Pro Lys Gly Ser Gln Gly Asp Pro Gly Arg Pro  
 545 550 555 560  
 Gly Glu Pro Gly Leu Pro Gly Ala Arg Gly Leu Thr Gly Asn Pro Gly  
 565 570 575  
 Val Gln Gly Pro Glu Gly Lys Leu Gly Pro Leu Gly Ala Pro Gly Glu  
 580 585 590  
 Asp Gly Arg Pro Gly Pro Pro Gly Ser Ile Gly Ile Lys Gly Gln Pro  
 595 600 605  
 Gly Thr Met Gly Leu Pro Gly Pro Lys Gly Ser Asn Gly Asp Pro Gly  
 610 615 620  
 Lys Pro Gly Glu Ala Gly Asn Pro Gly Val Pro Gly Gln Arg Gly Ala  
 625 630 635 640  
 Pro Gly Lys Asp Gly Lys Val Gly Pro Tyr Gly Pro Pro Gly Pro Pro  
 645 650 655  
 Gly Leu Arg Gly Glu Arg Gly Glu Gln Gly Pro Pro Gly Pro Thr Gly  
 660 665 670  
 Phe Gln Gly His Pro Gly Pro Pro Gly Pro Pro Gly Glu Gly Lys  
 675 680 685  
 Pro Gly Asp Gln Gly Val Pro Gly Gly Pro Gly Ala Val Gly Pro Leu  
 690 695 700  
 Gly Pro Arg Gly Glu Arg Gly Asn Pro Gly Glu Arg Gly Glu Pro Gly  
 705 710 715 720  
 Ile Thr Gly Leu Pro Gly Glu Lys Gly Met Ala Gly Gly His Gly Pro  
 725 730 735  
 Asp Gly Pro Lys Gly Ser Pro Gly Pro Ser Gly Thr Pro Gly Asp Thr  
 740 745 750  
 Gly Pro Pro Gly Leu Gln Gly Met Pro Gly Glu Arg Gly Ile Ala Gly  
 755 760 765  
 Thr Pro Gly Pro Lys Gly Asp Arg Gly Gly Ile Gly Glu Lys Gly Ala  
 770 775 780  
 Glu Gly Thr Ala Gly Asn Asp Gly Ala Gly Gly Leu Pro Gly Pro Leu  
 785 790 795 800  
 Gly Pro Pro Gly Pro Ala Gly Leu Leu Gly Glu Lys Gly Glu Pro Gly  
 805 810 815  
 Pro Arg Gly Leu Val Gly Pro Pro Gly Ser Arg Gly Asn Pro Gly Ser  
 820 825 830  
 Arg Gly Glu Asn Gly Pro Thr Gly Ala Val Gly Phe Ala Gly Pro Gln  
 835 840 845

Gly	Ser	Asp	Gly	Gln	Pro	Gly	Val	Lys	Gly	Glu	Pro	Gly	Glu	Pro	Gly		
850						855					860						
Gln	Lys	Gly	Asp	Ala	Gly	Ser	Pro	Gly	Pro	Gln	Gly	Leu	Ala	Gly	Ser		
865					870					875					880		
Pro	Gly	Pro	His	Gly	Pro	Asn	Gly	Val	Pro	Gly	Leu	Lys	Gly	Gly	Arg		
				885					890						895		
Gly	Thr	Gln	Gly	Pro	Pro	Gly	Ala	Thr	Gly	Phe	Pro	Gly	Ser	Ala	Gly		
		900					905						910				
Arg	Val	Gly	Pro	Pro	Gly	Pro	Ala	Gly	Ala	Pro	Gly	Pro	Ala	Gly	Pro		
		915					920					925					
Leu	Gly	Glu	Pro	Gly	Lys	Glu	Gly	Pro	Pro	Gly	Pro	Arg	Gly	Asp	Pro		
		930				935					940						
Gly	Ser	His	Gly	Arg	Val	Gly	Val	Arg	Gly	Pro	Ala	Gly	Pro	Pro	Gly		
945					950					955					960		
Gly	Pro	Gly	Asp	Lys	Gly	Asp	Pro	Gly	Glu	Asp	Gly	Gln	Pro	Gly	Pro		
				965					970						975		
Asp	Gly	Pro	Pro	Gly	Pro	Ala	Gly	Thr	Gly	Gln	Arg	Gly	Ile	Val			
		980						985					990				
Gly	Met	Pro	Gly	Gln	Arg	Gly	Glu	Arg	Gly	Met	Pro	Gly	Leu	Pro	Gly		
		995					1000					1005					
Pro	Ala	Gly	Thr	Pro	Gly	Lys	Val	Gly	Pro	Thr	Gly	Ala	Thr	Gly			
	1010					1015					1020						
Asp	Lys	Gly	Pro	Pro	Gly	Pro	Val	Gly	Pro	Pro	Gly	Ser	Asn	Gly			
	1025					1030					1035						
Pro	Val	Gly	Glu	Pro	Gly	Pro	Glu	Gly	Pro	Ala	Gly	Asn	Asp	Gly			
	1040					1045					1050						
Thr	Pro	Gly	Arg	Asp	Gly	Ala	Val	Gly	Glu	Arg	Gly	Asp	Arg	Gly			
	1055					1060					1065						
Asp	Pro	Gly	Pro	Ala	Gly	Leu	Pro	Gly	Ser	Gln	Gly	Ala	Pro	Gly			
	1070					1075					1080						
Thr	Pro	Gly	Pro	Val	Gly	Ala	Pro	Gly	Asp	Ala	Gly	Gln	Arg	Gly			
	1085					1090					1095						
Asp	Pro	Gly	Ser	Arg	Gly	Pro	Ile	Gly	His	Leu	Gly	Arg	Ala	Gly			
	1100					1105					1110						
Lys	Arg	Gly	Leu	Pro	Gly	Pro	Gln	Gly	Pro	Arg	Gly	Asp	Lys	Gly			
	1115					1120					1125						
Asp	His	Gly	Asp	Arg	Gly	Asp	Arg	Gly	Gln	Lys	Gly	His	Arg	Gly			
	1130					1135					1140						
Phe	Thr	Gly	Leu	Gln	Gly	Leu	Pro	Gly	Pro	Pro	Gly	Pro	Asn	Gly			
	1145					1150					1155						
Glu	Gln	Gly	Ser	Ala	Gly	Ile	Pro	Gly	Pro	Phe	Gly	Pro	Arg	Gly			
	1160					1165					1170						
Pro	Pro	Gly	Pro	Val	Gly	Pro	Ser	Gly	Lys	Glu	Gly	Asn	Pro	Gly			
	1175					1180					1185						
Pro	Leu	Gly	Pro	Leu	Gly	Pro	Pro	Gly	Val	Arg	Gly	Ser	Val	Gly			
	1190					1195					1200						
Glu	Ala	Gly	Pro	Glu	Gly	Pro	Pro	Gly	Glu	Pro	Gly	Pro	Pro	Gly			
	1205					1210					1215						
Pro	Pro	Gly	Pro	Pro	Gly	His	Leu	Thr	Ala	Ala	Leu	Gly	Asp	Ile			
	1220					1225					1230						
Met	Gly	His	Tyr	Asp	Glu	Ser	Met	Pro	Asp	Pro	Leu	Pro	Glu	Phe			
	1235					1240					1245						
Thr	Glu	Asp	Gln	Ala	Ala	Pro	Asp	Asp	Lys	Asn	Lys	Thr	Asp	Pro			
	1250					1255					1260						
Gly	Val	His	Ala	Thr	Leu	Lys	Ser	Leu	Ser	Ser	Gln	Ile	Glu	Thr			
	1265					1270					1275						
Met	Arg	Ser	Pro	Asp	Gly	Ser	Lys	Lys	His	Pro	Ala	Arg	Thr	Cys			
	1280					1285					1290						
Asp	Asp	Leu	Lys	Leu	Cys	His	Ser	Ala	Lys	Gln	Ser	Gly	Glu	Tyr			
	1295					1300					1305						
Trp	Ile	Asp	Pro	Asn	Gln	Gly	Ser	Val	Glu	Asp	Ala	Ile	Lys	Val			
	1310					1315					1320						

Tyr Cys Asn Met Glu Thr Gly Glu Thr Cys Ile Ser Ala Asn Pro  
 1325 1330 1335  
 Ser Ser Val Pro Arg Lys Thr Trp Trp Ala Ser Lys Ser Pro Asp  
 1340 1345 1350  
 Asn Lys Pro Val Trp Tyr Gly Leu Asp Met Asn Arg Gly Ser Gln  
 1355 1360 1365  
 Phe Ala Tyr Gly Asp His Gln Ser Pro Asn Thr Ala Ile Thr Gln  
 1370 1375 1380  
 Met Thr Phe Leu Arg Leu Leu Ser Lys Glu Ala Ser Gln Asn Ile  
 1385 1390 1395  
 Thr Tyr Ile Cys Lys Asn Ser Val Gly Tyr Met Asp Asp Gln Ala  
 1400 1405 1410  
 Lys Asn Leu Lys Lys Ala Val Val Leu Lys Gly Ala Asn Asp Leu  
 1415 1420 1425  
 Asp Ile Lys Ala Glu Gly Asn Ile Arg Phe Arg Tyr Ile Val Leu  
 1430 1435 1440  
 Gln Asp Thr Cys Ser Lys Arg Asn Gly Asn Val Gly Lys Thr Val  
 1445 1450 1455  
 Phe Glu Tyr Arg Thr Gln Asn Val Ala Arg Leu Pro Ile Ile Asp  
 1460 1465 1470  
 Leu Ala Pro Val Asp Val Gly Gly Thr Asp Gln Glu Phe Gly Val  
 1475 1480 1485  
 Glu Ile Gly Pro Val Cys Phe Val  
 1490 1495

&lt;210&gt; 310

&lt;211&gt; 52

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 310

Met Lys Arg Lys Thr Lys Thr Pro Ser Glu Gly Gly Gln Val Leu Ala  
 1 5 10 15  
 Glu Gln Arg Gly Ser Arg Ser Cys Gln Arg Leu Thr Ala Arg Lys Ala  
 20 25 30  
 Leu Pro Ile Leu Val Phe Thr Ile Glu Thr Ala Thr Ala Cys Thr Asp  
 35 40 45  
 His Phe Gly Ser  
 50

&lt;210&gt; 311

&lt;211&gt; 330

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 311

Met Ala Glu Glu Asp Leu Ala Pro Gly Lys Ser Ser Val Ala Val Asn  
 1 5 10 15  
 Asn Cys Ile Arg Gln Leu Ser Tyr Cys Lys Asn Asp Ile Arg Asp Thr  
 20 25 30  
 Val Gly Ile Trp Gly Glu Gly Lys Asp Met Tyr Leu Ile Leu Glu Asn  
 35 40 45

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Asp Met Leu Ser Leu Val Asp Pro Met Asp Arg Ser Val Leu His Ser  
 50 55 60  
 Gln Pro Ile Val Ser Ile Arg Val Trp Gly Val Gly Arg Asp Asn Gly  
 65 70 75 80  
 Arg Asp Phe Ala Tyr Val Ala Arg Asp Lys Asp Thr Arg Ile Leu Lys  
 85 90 95  
 Cys His Val Phe Arg Cys Asp Thr Pro Ala Lys Ala Ile Ala Thr Ser  
 100 105 110  
 Leu His Glu Ile Cys Ser Lys Ile Met Ala Glu Arg Lys Asn Ala Lys  
 115 120 125  
 Ala Leu Ala Cys Ser Ser Leu Gln Glu Arg Ala Asn Val Asn Leu Asp  
 130 135 140  
 Val Pro Leu Gln Val Asp Phe Pro Thr Pro Lys Thr Glu Leu Val Gln  
 145 150 155 160  
 Lys Phe His Val Gln Tyr Leu Gly Met Leu Pro Val Asp Lys Pro Val  
 165 170 175  
 Gly Met Asp Ile Leu Asn Ser Ala Ile Glu Asn Leu Met Thr Ser Ser  
 180 185 190  
 Asn Lys Glu Asp Trp Leu Ser Val Asn Met Asn Val Ala Asp Ala Thr  
 195 200 205  
 Val Thr Val Ile Ser Glu Lys Asn Glu Glu Glu Val Leu Val Glu Cys  
 210 215 220  
 Arg Val Arg Phe Leu Ser Phe Met Gly Val Gly Lys Asp Val His Thr  
 225 230 235 240  
 Phe Ala Phe Ile Met Asp Thr Gly Asn Gln Arg Phe Glu Cys His Val  
 245 250 255  
 Phe Trp Cys Glu Pro Asn Ala Gly Asn Val Ser Glu Ala Val Gln Ala  
 260 265 270  
 Ala Cys Met Leu Arg Tyr Gln Lys Cys Leu Val Ala Arg Pro Pro Ser  
 275 280 285  
 Gln Lys Val Arg Pro Pro Pro Pro Pro Ala Asp Ser Val Thr Arg Arg  
 290 295 300  
 Val Thr Thr Asn Val Lys Arg Gly Val Leu Ser Leu Ile Asp Thr Leu  
 305 310 315 320  
 Lys Gln Lys Arg Pro Val Thr Glu Met Pro  
 325 330

&lt;210&gt; 312

&lt;211&gt; 115

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 312

Met Ser Arg His Ser Arg Leu Gln Arg Gln Val Leu Ser Leu Tyr Arg  
 1 5 10 15  
 Asp Leu Leu Arg Ala Gly Arg Gly Lys Pro Gly Ala Glu Ala Arg Val  
 20 25 30  
 Arg Ala Glu Phe Arg Gln His Ala Gly Leu Pro Arg Ser Asp Val Leu  
 35 40 45  
 Arg Ile Glu Tyr Leu Tyr Arg Arg Gly Arg Arg Gln Leu Gln Leu Leu  
 50 55 60  
 Arg Ser Gly His Ala Thr Ala Met Gly Ala Phe Val Arg Pro Arg Ala  
 65 70 75 80  
 Pro Thr Gly Glu Pro Gly Gly Val Gly Cys Gln Pro Asp Asp Gly Asp  
 85 90 95

Ser Pro Arg Asn Pro His Asp Ser Thr Gly Ala Pro Glu Thr Arg Pro  
 100 105 110  
 Asp Gly Arg 115

<210> 313

<211> 321

<212> PRT

<213> Homo sapiens

<400> 313

Met Lys Glu Asp Cys Leu Pro Ser Ser His Val Pro Ile Ser Asp Ser  
 1 5 10 15  
 Lys Ser Ile Gln Lys Ser Glu Leu Leu Gly Leu Leu Lys Thr Tyr Asn  
 20 25 30  
 Cys Tyr His Glu Gly Lys Ser Phe Gln Leu Arg His Arg Glu Glu Glu  
 35 40 45  
 Gly Thr Leu Ile Ile Glu Gly Leu Leu Asn Ile Ala Trp Gly Leu Arg  
 50 55 60  
 Arg Pro Ile Arg Leu Gln Met Gln Asp Asp Arg Glu Gln Val His Leu  
 65 70 75 80  
 Pro Ser Thr Ser Trp Met Pro Arg Arg Pro Ser Cys Pro Leu Lys Glu  
 85 90 95  
 Pro Ser Pro Gln Asn Gly Asn Ile Thr Ala Gln Gly Pro Ser Ile Gln  
 100 105 110  
 Pro Val His Lys Ala Glu Ser Ser Thr Asp Ser Ser Gly Pro Leu Glu  
 115 120 125  
 Glu Ala Glu Glu Ala Pro Gln Leu Met Arg Thr Lys Ser Asp Ala Ser  
 130 135 140  
 Cys Met Ser Gln Arg Arg Pro Lys Cys Arg Ala Pro Gly Glu Ala Gln  
 145 150 155 160  
 Arg Ile Arg Arg His Arg Phe Ser Ile Asn Gly His Phe Tyr Asn His  
 165 170 175  
 Lys Thr Ser Val Phe Thr Pro Ala Tyr Gly Ser Val Thr Asn Val Arg  
 180 185 190  
 Val Asn Ser Thr Met Thr Thr Leu Gln Val Leu Thr Leu Leu Asn  
 195 200 205  
 Lys Phe Arg Val Glu Asp Gly Pro Ser Glu Phe Ala Leu Tyr Ile Val  
 210 215 220  
 His Glu Ser Gly Glu Arg Thr Lys Leu Lys Asp Cys Glu Tyr Pro Leu  
 225 230 235 240  
 Ile Ser Arg Ile Leu His Gly Pro Cys Glu Lys Ile Ala Arg Ile Phe  
 245 250 255  
 Leu Met Glu Ala Asp Leu Gly Val Glu Val Pro His Glu Val Ala Gln  
 260 265 270  
 Tyr Ile Lys Phe Glu Met Pro Val Leu Asp Ser Phe Val Glu Lys Leu  
 275 280 285  
 Lys Glu Glu Glu Glu Arg Glu Ile Ile Lys Leu Thr Met Lys Phe Gln  
 290 295 300  
 Ala Leu Arg Leu Thr Met Leu Gln Arg Leu Glu Gln Leu Val Glu Ala  
 305 310 315 320  
 Lys

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&lt;210&gt; 314

&lt;211&gt; 490

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 314

Met	Trp	Pro	Gln	Asp	Pro	Ser	Arg	Lys	Glu	Val	Leu	Arg	Phe	Ala	Val
1				5					10					15	
Ser	Cys	Arg	Ile	Leu	Thr	Leu	Met	Leu	Gln	Ala	Leu	Phe	Asn	Ala	Ile
			20					25					30		
Ile	Pro	Asp	His	His	Ala	Glu	Ala	Phe	Ser	Pro	Pro	Arg	Leu	Ala	Pro
		35					40					45			
Ser	Gly	Phe	Val	Asp	Gln	Leu	Val	Glu	Gly	Leu	Leu	Gly	Gly	Leu	Ser
	50					55					60				
His	Trp	Asp	Ala	Glu	His	Phe	Leu	Phe	Ile	Ala	Glu	His	Gly	Tyr	Leu
65					70					75					80
Tyr	Glu	His	Asn	Phe	Ala	Phe	Phe	Pro	Gly	Phe	Pro	Leu	Ala	Leu	Leu
			85						90					95	
Val	Gly	Thr	Glu	Leu	Leu	Arg	Pro	Leu	Arg	Gly	Leu	Leu	Ser	Leu	Arg
			100					105					110		
Ser	Cys	Leu	Leu	Ile	Ser	Val	Ala	Ser	Leu	Asn	Phe	Leu	Phe	Phe	Met
		115					120					125			
Leu	Ala	Ala	Val	Ala	Leu	His	Asp	Leu	Gly	Cys	Leu	Val	Leu	His	Cys
	130					135					140				
Pro	His	Gln	Ser	Phe	Tyr	Ala	Ala	Leu	Leu	Phe	Cys	Leu	Ser	Pro	Ala
145					150					155					160
Asn	Val	Phe	Leu	Ala	Ala	Gly	Tyr	Ser	Glu	Ala	Leu	Phe	Ala	Leu	Leu
			165						170					175	
Thr	Phe	Ser	Ala	Met	Gly	Gln	Leu	Glu	Arg	Gly	Arg	Val	Trp	Thr	Ser
			180					185					190		
Val	Leu	Leu	Phe	Ala	Phe	Ala	Thr	Gly	Val	Arg	Ser	Asn	Gly	Leu	Val
	195						200					205			
Ser	Val	Gly	Phe	Leu	Met	His	Ser	Gln	Cys	Gln	Gly	Phe	Phe	Ser	Ser
	210					215					220				
Leu	Thr	Met	Leu	Asn	Pro	Leu	Arg	Gln	Leu	Phe	Lys	Leu	Met	Ala	Ser
225				230						235					240
Leu	Phe	Leu	Ser	Val	Phe	Thr	Leu	Gly	Leu	Pro	Phe	Ala	Leu	Phe	Gln
			245					250						255	
Tyr	Tyr	Ala	Tyr	Thr	Gln	Phe	Cys	Leu	Pro	Gly	Ser	Ala	Arg	Pro	Ile
			260					265					270		
Pro	Glu	Pro	Leu	Val	Gln	Leu	Ala	Val	Asp	Lys	Gly	Tyr	Arg	Ile	Ala
		275					280					285			
Glu	Gly	Asn	Glu	Pro	Pro	Trp	Cys	Phe	Trp	Asp	Val	Pro	Leu	Ile	Tyr
	290					295					300				
Ser	Tyr	Ile	Gln	Asp	Val	Tyr	Trp	Asn	Val	Gly	Phe	Leu	Lys	Tyr	Tyr
305					310					315					320
Glu	Leu	Lys	Gln	Val	Pro	Asn	Phe	Leu	Leu	Ala	Ala	Pro	Val	Ala	Ile
			325						330					335	
Leu	Val	Ala	Trp	Ala	Thr	Trp	Thr	Tyr	Val	Thr	Thr	His	Pro	Trp	Leu
			340					345					350		
Cys	Leu	Thr	Leu	Gly	Leu	Gln	Arg	Ser	Lys	Asn	Asn	Lys	Thr	Leu	Glu
		355					360					365			
Lys	Pro	Asp	Leu	Gly	Phe	Leu	Ser	Pro	Gln	Val	Phe	Val	Tyr	Val	Val
	370					375					380				
His	Ala	Ala	Val	Leu	Leu	Phe	Gly	Gly	Leu	Cys	Met	His	Val	Gln	
385					390				395					400	



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Val Leu Thr Arg Phe Leu Gly Ser Ser Thr Pro Ile Met Tyr Trp Phe  
 405 410 415  
 Pro Ala His Leu Leu Gln Asp Gln Glu Pro Leu Leu Arg Ser Leu Lys  
 420 425 430  
 Thr Val Pro Trp Lys Pro Leu Ala Glu Asp Ser Pro Pro Gly Gln Lys  
 435 440 445  
 Val Pro Arg Asn Pro Ile Met Gly Leu Leu Tyr His Trp Lys Thr Cys  
 450 455 460  
 Ser Pro Val Thr Arg Tyr Ile Leu Gly Tyr Phe Leu Thr Tyr Trp Leu  
 465 470 475 480  
 Leu Gly Leu Leu Leu His Cys Asn Phe Leu  
 485 490

&lt;210&gt; 315

&lt;211&gt; 688

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 315  
 Met Ser Ser Arg Thr Val Leu Ala Pro Gly Asn Asp Arg Asn Ser Asp  
 1 5 10 15  
 Thr His Gly Thr Leu Gly Ser Gly Arg Ser Ser Asp Lys Gly Pro Ser  
 20 25 30  
 Trp Ser Ser Arg Ser Leu Gly Ala Arg Cys Arg Asn Ser Ile Ala Ser  
 35 40 45  
 Cys Pro Glu Glu Gln Pro His Val Gly Asn Tyr Arg Leu Leu Arg Thr  
 50 55 60  
 Ile Gly Lys Gly Asn Phe Ala Lys Val Lys Leu Ala Arg His Ile Leu  
 65 70 75 80  
 Thr Gly Arg Glu Val Ala Ile Lys Ile Ile Asp Lys Thr Gln Leu Asn  
 85 90 95  
 Pro Ser Ser Leu Gln Lys Leu Phe Arg Glu Val Arg Ile Met Lys Gly  
 100 105 110  
 Leu Asn His Pro Asn Ile Val Lys Leu Phe Glu Val Ile Glu Thr Glu  
 115 120 125  
 Lys Thr Leu Tyr Leu Val Met Glu Tyr Ala Ser Ala Gly Glu Val Phe  
 130 135 140  
 Asp Tyr Leu Val Ser His Gly Arg Met Lys Glu Lys Glu Ala Arg Ala  
 145 150 155 160  
 Lys Phe Arg Gln Ile Val Ser Ala Val His Tyr Cys His Gln Lys Asn  
 165 170 175  
 Ile Val His Arg Asp Leu Lys Ala Glu Asn Leu Leu Leu Asp Ala Glu  
 180 185 190  
 Ala Asn Ile Lys Ile Ala Asp Phe Gly Phe Ser Asn Glu Phe Thr Leu  
 195 200 205  
 Gly Ser Lys Leu Asp Thr Phe Cys Gly Ser Pro Pro Tyr Ala Ala Pro  
 210 215 220  
 Glu Leu Phe Gln Gly Lys Lys Tyr Asp Gly Pro Glu Val Asp Ile Trp  
 225 230 235 240  
 Ser Leu Gly Val Ile Leu Tyr Thr Leu Val Ser Gly Ser Leu Pro Phe  
 245 250 255  
 Asp Gly His Asn Leu Lys Glu Leu Arg Glu Arg Val Leu Arg Gly Lys  
 260 265 270  
 Tyr Arg Val Pro Phe Tyr Met Ser Thr Asp Cys Glu Ser Ile Leu Arg  
 275 280 285  
 Arg Phe Leu Val Leu Asn Pro Ala Lys Arg Cys Thr Leu Glu Gln Ile  
 290 295 300

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Met Lys Asp Lys Trp Ile Asn Ile Gly Tyr Glu Gly Glu Glu Leu Lys
305                               310           315           320
Pro Tyr Thr Glu Pro Glu Glu Asp Phe Gly Asp Thr Lys Arg Ile Glu
                               325           330           335
Val Met Val Gly Met Gly Tyr Thr Arg Glu Glu Ile Lys Glu Ser Leu
                               340           345           350
Thr Ser Gln Lys Tyr Asn Glu Val Thr Ala Thr Tyr Leu Leu Leu Gly
                               355           360           365
Arg Lys Thr Glu Glu Gly Gly Asp Arg Gly Ala Pro Gly Leu Ala Leu
                               370           375           380
Ala Arg Val Arg Ala Pro Ser Asp Thr Thr Asn Gly Thr Ser Ser Ser
385                               390           395           400
Lys Gly Thr Ser His Ser Lys Gly Gln Arg Ser Ser Ser Ser Thr Tyr
                               405           410           415
His Arg Gln Arg Arg His Ser Asp Phe Cys Gly Pro Ser Pro Ala Pro
                               420           425           430
Leu His Pro Lys Arg Ser Pro Thr Ser Thr Gly Glu Ala Glu Leu Lys
                               435           440           445
Glu Glu Arg Leu Pro Gly Arg Lys Ala Ser Cys Ser Thr Ala Gly Ser
450                               455           460           465
Gly Ser Arg Gly Leu Pro Pro Ser Ser Pro Met Val Ser Ser Ala His
465                               470           475           480
Asn Pro Asn Lys Ala Glu Ile Pro Glu Arg Arg Lys Asp Ser Thr Ser
                               485           490           495
Thr Pro Asn Asn Leu Pro Pro Ser Met Met Thr Arg Arg Asn Thr Tyr
                               500           505           510
Val Cys Thr Glu Arg Pro Gly Ala Glu Arg Pro Ser Leu Leu Pro Asn
                               515           520           525
Gly Lys Glu Asn Ser Ser Gly Thr Pro Arg Val Pro Pro Ala Ser Pro
                               530           535           540
Ser Ser His Ser Leu Ala Pro Pro Ser Gly Glu Arg Ser Arg Leu Ala
545                               550           555           560
Arg Gly Ser Thr Ile Arg Ser Thr Phe His Gly Gly Gln Val Arg Asp
                               565           570           575
Arg Arg Ala Gly Gly Gly Gly Gly Gly Gly Val Gln Asn Gly Pro Pro
                               580           585           590
Ala Ser Pro Thr Leu Ala His Glu Ala Ala Pro Leu Pro Ala Gly Arg
                               595           600           605
Pro Arg Pro Thr Thr Asn Leu Phe Thr Lys Leu Thr Ser Lys Leu Thr
610                               615           620
Arg Arg Val Thr Leu Asp Pro Ser Lys Arg Gln Asn Ser Asn Arg Cys
625                               630           635           640
Val Ser Gly Ala Ser Leu Pro Gln Gly Ser Lys Ile Arg Ser Gln Thr
                               645           650           655
Asn Leu Arg Glu Ser Gly Asp Leu Arg Ser Gln Val Ala Ile Tyr Leu
660                               665           670
Gly Ile Lys Arg Lys Pro Pro Pro Gly Cys Ser Asp Ser Pro Gly Val
675                               680           685

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&lt;210&gt; 316

&lt;211&gt; 338

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 316

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Met Ser Leu Ser Ala Phe Thr Leu Phe Leu Ala Leu Ile Gly Gly Thr
1          5          10          15

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Ser Gly Gln Tyr Tyr Asp Tyr Asp Phe Pro Leu Ser Ile Tyr Gly Gln  
 20 25 30  
 Ser Ser Pro Asn Cys Ala Pro Glu Cys Asn Cys Pro Glu Ser Tyr Pro  
 35 40 45  
 Ser Ala Met Tyr Cys Asp Glu Leu Lys Leu Lys Ser Val Pro Met Val  
 50 55 60  
 Pro Pro Gly Ile Lys Tyr Leu Tyr Leu Arg Asn Asn Gln Ile Asp His  
 65 70 75 80  
 Ile Asp Glu Lys Ala Phe Glu Asn Val Thr Asp Leu Gln Trp Leu Ile  
 85 90 95  
 Leu Asp His Asn Leu Leu Glu Asn Ser Lys Ile Lys Gly Arg Val Phe  
 100 105 110  
 Ser Lys Leu Lys Gln Leu Lys Lys Leu His Ile Asn His Asn Asn Leu  
 115 120 125  
 Thr Glu Ser Val Gly Pro Leu Pro Lys Ser Leu Glu Asp Leu Gln Leu  
 130 135 140  
 Thr His Asn Lys Ile Thr Lys Leu Gly Ser Phe Glu Gly Leu Val Asn  
 145 150 155 160  
 Leu Thr Phe Ile His Leu Gln His Asn Arg Leu Lys Glu Asp Ala Val  
 165 170 175  
 Ser Ala Ala Phe Lys Gly Leu Lys Ser Leu Glu Tyr Leu Asp Leu Ser  
 180 185 190  
 Phe Asn Gln Ile Ala Arg Leu Pro Ser Gly Leu Pro Val Ser Leu Leu  
 195 200 205  
 Thr Leu Tyr Leu Asp Asn Asn Lys Ile Ser Asn Ile Pro Asp Glu Tyr  
 210 215 220  
 Phe Lys Arg Phe Asn Ala Leu Gln Tyr Leu Arg Leu Ser His Asn Glu  
 225 230 235 240  
 Leu Ala Asp Ser Gly Ile Pro Gly Asn Ser Phe Asn Val Ser Ser Leu  
 245 250 255  
 Val Glu Leu Asp Leu Ser Tyr Asn Lys Leu Lys Asn Ile Pro Thr Val  
 260 265 270  
 Asn Glu Asn Leu Glu Asn Tyr Tyr Leu Glu Val Asn Gln Leu Glu Lys  
 275 280 285  
 Phe Asp Ile Lys Ser Phe Cys Lys Ile Leu Gly Pro Leu Ser Tyr Ser  
 290 295 300  
 Lys Ile Lys His Leu Arg Leu Asp Gly Asn Arg Ile Ser Glu Thr Ser  
 305 310 315 320  
 Leu Pro Pro Asp Met Tyr Glu Cys Leu Arg Val Ala Asn Glu Val Thr  
 325 330 335  
 Leu Asn

&lt;210&gt; 317

&lt;211&gt; 1466

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 317

Met Met Ser Phe Val Gln Lys Gly Ser Trp Leu Leu Leu Ala Leu Leu  
 1 5 10 15  
 His Pro Thr Ile Ile Leu Ala Gln Gln Glu Ala Val Glu Gly Gly Cys  
 20 25 30  
 Ser His Leu Gly Gln Ser Tyr Ala Asp Arg Asp Val Trp Lys Pro Glu  
 35 40 45  
 Pro Cys Gln Ile Cys Val Cys Asp Ser Gly Ser Val Leu Cys Asp Asp  
 50 55 60

Ile	Ile	Cys	Asp	Asp	Gln	Glu	Leu	Asp	Cys	Pro	Asn	Pro	Glu	Ile	Pro
65					70					75					80
Phe	Gly	Glu	Cys	Cys	Ala	Val	Cys	Pro	Gln	Pro	Pro	Thr	Ala	Pro	Thr
				85					90					95	
Arg	Pro	Pro	Asn	Gly	Gln	Gly	Pro	Gln	Gly	Pro	Lys	Gly	Asp	Pro	Gly
			100					105					110		
Pro	Pro	Gly	Ile	Pro	Gly	Arg	Asn	Gly	Asp	Pro	Gly	Ile	Pro	Gly	Gln
		115					120					125			
Pro	Gly	Ser	Pro	Gly	Ser	Pro	Gly	Pro	Pro	Gly	Ile	Cys	Glu	Ser	Cys
	130					135					140				
Pro	Thr	Gly	Pro	Gln	Asn	Tyr	Ser	Pro	Gln	Tyr	Asp	Ser	Tyr	Asp	Val
145				150						155					160
Lys	Ser	Gly	Val	Ala	Val	Gly	Gly	Leu	Ala	Gly	Tyr	Pro	Gly	Pro	Ala
			165						170					175	
Gly	Pro	Pro	Gly	Pro	Pro	Gly	Pro	Pro	Gly	Thr	Ser	Gly	His	Pro	Gly
		180						185					190		
Ser	Pro	Gly	Ser	Pro	Gly	Tyr	Gln	Gly	Pro	Pro	Gly	Glu	Pro	Gly	Gln
	195						200					205			
Ala	Gly	Pro	Ser	Gly	Pro	Pro	Gly	Pro	Pro	Gly	Ala	Ile	Gly	Pro	Ser
	210					215					220				
Gly	Pro	Ala	Gly	Lys	Asp	Gly	Glu	Ser	Gly	Arg	Pro	Gly	Arg	Pro	Gly
225				230						235					240
Glu	Arg	Gly	Leu	Pro	Gly	Pro	Pro	Gly	Ile	Lys	Gly	Pro	Ala	Gly	Ile
			245						250					255	
Pro	Gly	Phe	Pro	Gly	Met	Lys	Gly	His	Arg	Gly	Phe	Asp	Gly	Arg	Asn
		260						265					270		
Gly	Glu	Lys	Gly	Glu	Thr	Gly	Ala	Pro	Gly	Leu	Lys	Gly	Glu	Asn	Gly
	275						280					285			
Leu	Pro	Gly	Glu	Asn	Gly	Ala	Pro	Gly	Pro	Met	Gly	Pro	Arg	Gly	Ala
	290					295					300				
Pro	Gly	Glu	Arg	Gly	Arg	Pro	Gly	Leu	Pro	Gly	Ala	Ala	Gly	Ala	Arg
305				310						315					320
Gly	Asn	Asp	Gly	Ala	Arg	Gly	Ser	Asp	Gly	Gln	Pro	Gly	Pro	Pro	Gly
			325						330					335	
Pro	Pro	Gly	Thr	Ala	Gly	Phe	Pro	Gly	Ser	Pro	Gly	Ala	Lys	Gly	Glu
		340						345					350		
Val	Gly	Pro	Ala	Gly	Ser	Pro	Gly	Ser	Asn	Gly	Ala	Pro	Gly	Gln	Arg
	355						360					365			
Gly	Glu	Pro	Gly	Pro	Gln	Gly	His	Ala	Gly	Ala	Gln	Gly	Pro	Pro	Gly
	370					375					380				
Pro	Pro	Gly	Ile	Asn	Gly	Ser	Pro	Gly	Gly	Lys	Gly	Glu	Met	Gly	Pro
385				390						395					400
Ala	Gly	Ile	Pro	Gly	Ala	Pro	Gly	Leu	Met	Gly	Ala	Arg	Gly	Pro	Pro
			405						410					415	
Gly	Pro	Ala	Gly	Ala	Asn	Gly	Ala	Pro	Gly	Leu	Arg	Gly	Gly	Ala	Gly
		420						425					430		
Glu	Pro	Gly	Lys	Asn	Gly	Ala	Lys	Gly	Glu	Pro	Gly	Pro	Arg	Gly	Glu
	435						440					445			
Arg	Gly	Glu	Ala	Gly	Ile	Pro	Gly	Val	Pro	Gly	Ala	Lys	Gly	Glu	Asp
	450					455					460				
Gly	Lys	Asp	Gly	Ser	Pro	Gly	Glu	Pro	Gly	Ala	Asn	Gly	Leu	Pro	Gly
465				470						475					480
Ala	Ala	Gly	Glu	Arg	Gly	Ala	Pro	Gly	Phe	Arg	Gly	Pro	Ala	Gly	Pro
			485						490					495	
Asn	Gly	Ile	Pro	Gly	Glu	Lys	Gly	Pro	Ala	Gly	Glu	Arg	Gly	Ala	Pro
		500						505					510		
Gly	Pro	Ala	Gly	Pro	Arg	Gly	Ala	Ala	Gly	Glu	Pro	Gly	Arg	Asp	Gly
	515						520					525			
Val	Pro	Gly	Gly	Pro	Gly	Met	Arg	Gly	Met	Pro	Gly	Ser	Pro	Gly	Gly
	530					535					540				
Pro	Gly	Ser	Asp	Gly	Lys	Pro	Gly	Pro	Pro	Gly	Ser	Gln	Gly	Glu	Ser
545					550					555					560

Gly Arg Pro Gly Pro Pro Gly Pro Ser Gly Pro Arg Gly Gln Pro Gly  
 565 570 575  
 Val Met Gly Phe Pro Gly Pro Lys Gly Asn Asp Gly Ala Pro Gly Lys  
 580 585 590  
 Asn Gly Glu Arg Gly Gly Pro Gly Gly Pro Gly Pro Gln Gly Pro Pro  
 595 600 605  
 Gly Lys Asn Gly Glu Thr Gly Pro Gln Gly Pro Pro Gly Pro Thr Gly  
 610 615 620  
 Pro Gly Gly Asp Lys Gly Asp Thr Gly Pro Pro Gly Pro Gln Gly Leu  
 625 630 635 640  
 Gln Gly Leu Pro Gly Thr Gly Gly Pro Pro Gly Glu Asn Gly Lys Pro  
 645 650 655  
 Gly Glu Pro Gly Pro Lys Gly Asp Ala Gly Ala Pro Gly Ala Pro Gly  
 660 665 670  
 Gly Lys Gly Asp Ala Gly Ala Pro Gly Glu Arg Gly Pro Pro Gly Leu  
 675 680 685  
 Ala Gly Ala Pro Gly Leu Arg Gly Gly Ala Gly Pro Gly Pro Glu  
 690 695 700  
 Gly Gly Lys Gly Ala Ala Gly Pro Pro Gly Pro Pro Gly Ala Ala Gly  
 705 710 715 720  
 Thr Pro Gly Leu Gln Gly Met Pro Gly Glu Arg Gly Gly Leu Gly Ser  
 725 730 735  
 Pro Gly Pro Lys Gly Asp Lys Gly Glu Pro Gly Gly Pro Gly Ala Asp  
 740 745 750  
 Gly Val Pro Gly Lys Asp Gly Pro Arg Gly Pro Thr Gly Pro Ile Gly  
 755 760 765  
 Pro Pro Gly Pro Ala Gly Gln Pro Gly Asp Lys Gly Glu Gly Gly Ala  
 770 775 780  
 Pro Gly Leu Pro Gly Ile Ala Gly Pro Arg Gly Ser Pro Gly Glu Arg  
 785 790 795 800  
 Gly Glu Thr Gly Pro Pro Gly Pro Ala Gly Phe Pro Gly Ala Pro Gly  
 805 810 815  
 Gln Asn Gly Glu Pro Gly Gly Lys Gly Glu Arg Gly Ala Pro Gly Glu  
 820 825 830  
 Lys Gly Glu Gly Gly Pro Pro Gly Val Ala Gly Pro Pro Gly Gly Ser  
 835 840 845  
 Gly Pro Ala Gly Pro Pro Gly Pro Gln Gly Val Lys Gly Glu Arg Gly  
 850 855 860  
 Ser Pro Gly Gly Pro Gly Ala Ala Gly Phe Pro Gly Ala Arg Gly Leu  
 865 870 875 880  
 Pro Gly Pro Pro Gly Ser Asn Gly Asn Pro Gly Pro Pro Gly Pro Ser  
 885 890 895  
 Gly Ser Pro Gly Lys Asp Gly Pro Pro Gly Pro Ala Gly Asn Thr Gly  
 900 905 910  
 Ala Pro Gly Ser Pro Gly Val Ser Gly Pro Lys Gly Asp Ala Gly Gln  
 915 920 925  
 Pro Gly Glu Lys Gly Ser Pro Gly Ala Gln Gly Pro Pro Gly Ala Pro  
 930 935 940  
 Gly Pro Leu Gly Ile Ala Gly Ile Thr Gly Ala Arg Gly Leu Ala Gly  
 945 950 955 960  
 Pro Pro Gly Met Pro Gly Pro Arg Gly Ser Pro Gly Pro Gln Gly Val  
 965 970 975  
 Lys Gly Glu Ser Gly Lys Pro Gly Ala Asn Gly Leu Ser Gly Glu Arg  
 980 985 990  
 Gly Pro Pro Gly Pro Gln Gly Leu Pro Gly Leu Ala Gly Thr Ala Gly  
 995 1000 1005  
 Glu Pro Gly Arg Asp Gly Asn Pro Gly Ser Asp Gly Leu Pro Gly  
 1010 1015 1020  
 Arg Asp Gly Ser Pro Gly Gly Lys Gly Asp Arg Gly Glu Asn Gly  
 1025 1030 1035  
 Ser Pro Gly Ala Pro Gly Ala Pro Gly His Pro Gly Pro Pro Gly  
 1040 1045 1050

Pro Val	Gly Pro Ala Gly	Lys	Ser Gly Asp Arg	Gly	Glu Ser Gly
1055		1060		1065	
Pro Ala	Gly Pro Ala Gly	Ala	Pro Gly Pro Ala	Gly	Ser Arg Gly
1070		1075		1080	
Ala Pro	Gly Pro Gln Gly	Pro	Arg Gly Asp Lys	Gly	Glu Thr Gly
1085		1090		1095	
Glu Arg	Gly Ala Ala Gly	Ile	Lys Gly His Arg	Gly	Phe Pro Gly
1100		1105		1110	
Asn Pro	Gly Ala Pro Gly	Ser	Pro Gly Pro Ala	Gly	Gln Gln Gly
1115		1120		1125	
Ala Ile	Gly Ser Pro Gly	Pro	Ala Gly Pro Arg	Gly	Pro Val Gly
1130		1135		1140	
Pro Ser	Gly Pro Pro Gly	Lys	Asp Gly Thr Ser	Gly	His Pro Gly
1145		1150		1155	
Pro Ile	Gly Pro Pro Gly	Pro	Arg Gly Asn Arg	Gly	Glu Arg Gly
1160		1165		1170	
Ser Glu	Gly Ser Pro Gly	His	Pro Gly Gln Pro	Gly	Pro Pro Gly
1175		1180		1185	
Pro Pro	Gly Ala Pro Gly	Pro	Cys Cys Gly Gly	Val	Gly Ala Ala
1190		1195		1200	
Ala Ile	Ala Gly Ile Gly	Gly	Glu Lys Ala Gly	Gly	Phe Ala Pro
1205		1210		1215	
Tyr Tyr	Gly Asp Glu Pro	Met	Asp Phe Lys Ile	Asn	Thr Asp Glu
1220		1225		1230	
Ile Met	Thr Ser Leu Lys	Ser	Val Asn Gly Gln	Ile	Glu Ser Leu
1235		1240		1245	
Ile Ser	Pro Asp Gly Ser	Arg	Lys Asn Pro Ala	Arg	Asn Cys Arg
1250		1255		1260	
Asp Leu	Lys Phe Cys His	Pro	Glu Leu Lys Ser	Gly	Glu Tyr Trp
1265		1270		1275	
Val Asp	Pro Asn Gln Gly	Cys	Lys Leu Asp Ala	Ile	Lys Val Phe
1280		1285		1290	
Cys Asn	Met Glu Thr Gly	Glu	Thr Cys Ile Ser	Ala	Asn Pro Leu
1295		1300		1305	
Asn Val	Pro Arg Lys His	Trp	Trp Thr Asp Ser	Ser	Ala Glu Lys
1310		1315		1320	
Lys His	Val Trp Phe Gly	Glu	Ser Met Asp Gly	Gly	Phe Gln Phe
1325		1330		1335	
Ser Tyr	Gly Asn Pro Glu	Leu	Pro Glu Asp Val	Leu	Asp Val Gln
1340		1345		1350	
Leu Ala	Phe Leu Arg Leu	Leu	Ser Ser Arg Ala	Ser	Gln Asn Ile
1355		1360		1365	
Thr Tyr	His Cys Lys Asn	Ser	Ile Ala Tyr Met	Asp	Gln Ala Ser
1370		1375		1380	
Gly Asn	Val Lys Lys Ala	Leu	Lys Leu Met Gly	Ser	Asn Glu Gly
1385		1390		1395	
Glu Phe	Lys Ala Glu Gly	Asn	Ser Lys Phe Thr	Tyr	Thr Val Leu
1400		1405		1410	
Glu Asp	Gly Cys Thr Lys	His	Thr Gly Glu Trp	Ser	Lys Thr Val
1415		1420		1425	
Phe Glu	Tyr Arg Thr Arg	Lys	Ala Val Arg Leu	Pro	Ile Val Asp
1430		1435		1440	
Ile Ala	Pro Tyr Asp Ile	Gly	Gly Pro Asp Gln	Glu	Phe Gly Val
1445		1450		1455	
Asp Val	Gly Pro Val Cys	Phe	Leu		
1460		1465			

&lt;210&gt; 318

&lt;211&gt; 1464

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 318  
 Met Phe Ser Phe Val Asp Leu Arg Leu Leu Leu Leu Leu Ala Ala Thr  
 1 5 10 15  
 Ala Leu Leu Thr His Gly Gln Glu Glu Gly Gln Val Glu Gly Gln Asp  
 20 25 30  
 Glu Asp Ile Pro Pro Ile Thr Cys Val Gln Asn Gly Leu Arg Tyr His  
 35 40 45  
 Asp Arg Asp Val Trp Lys Pro Glu Pro Cys Arg Ile Cys Val Cys Asp  
 50 55 60  
 Asn Gly Lys Val Leu Cys Asp Asp Val Ile Cys Asp Glu Thr Lys Asn  
 65 70 75 80  
 Cys Pro Gly Ala Glu Val Pro Glu Gly Glu Cys Cys Pro Val Cys Pro  
 85 90 95  
 Asp Gly Ser Glu Ser Pro Thr Asp Gln Glu Thr Thr Gly Val Glu Gly  
 100 105 110  
 Pro Lys Gly Asp Thr Gly Pro Arg Gly Pro Arg Gly Pro Ala Gly Pro  
 115 120 125  
 Pro Gly Arg Asp Gly Ile Pro Gly Gln Pro Gly Leu Pro Gly Pro Pro  
 130 135 140  
 Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly Leu Gly Gly Asn Phe Ala  
 145 150 155 160  
 Pro Gln Leu Ser Tyr Gly Tyr Asp Glu Lys Ser Thr Gly Gly Ile Ser  
 165 170 175  
 Val Pro Gly Pro Met Gly Pro Ser Gly Pro Arg Gly Leu Pro Gly Pro  
 180 185 190  
 Pro Gly Ala Pro Gly Pro Gln Gly Phe Gln Gly Pro Pro Gly Glu Pro  
 195 200 205  
 Gly Glu Pro Gly Ala Ser Gly Pro Met Gly Pro Arg Gly Pro Pro Gly  
 210 215 220  
 Pro Pro Gly Lys Asn Gly Asp Asp Gly Glu Ala Gly Lys Pro Gly Arg  
 225 230 235 240  
 Pro Gly Glu Arg Gly Pro Pro Gly Pro Gln Gly Ala Arg Gly Leu Pro  
 245 250 255  
 Gly Thr Ala Gly Leu Pro Gly Met Lys Gly His Arg Gly Phe Ser Gly  
 260 265 270  
 Leu Asp Gly Ala Lys Gly Asp Ala Gly Pro Ala Gly Pro Lys Gly Glu  
 275 280 285  
 Pro Gly Ser Pro Gly Glu Asn Gly Ala Pro Gly Gln Met Gly Pro Arg  
 290 295 300  
 Gly Leu Pro Gly Glu Arg Gly Arg Pro Gly Ala Pro Gly Pro Ala Gly  
 305 310 315 320  
 Ala Arg Gly Asn Asp Gly Ala Thr Gly Ala Ala Gly Pro Pro Gly Pro  
 325 330 335  
 Thr Gly Pro Ala Gly Pro Pro Gly Phe Pro Gly Ala Val Gly Ala Lys  
 340 345 350  
 Gly Glu Ala Gly Pro Gln Gly Pro Arg Gly Ser Glu Gly Pro Gln Gly  
 355 360 365  
 Val Arg Gly Glu Pro Gly Pro Pro Gly Pro Ala Gly Ala Ala Gly Pro  
 370 375 380  
 Ala Gly Asn Pro Gly Ala Asp Gly Gln Pro Gly Ala Lys Gly Ala Asn  
 385 390 395 400

Gly Ala Pro Gly Ile Ala Gly Ala Pro Gly Phe Pro Gly Ala Arg Gly  
 405 410 415  
 Pro Ser Gly Pro Gln Gly Pro Gly Gly Pro Pro Gly Pro Lys Gly Asn  
 420 425 430  
 Ser Gly Glu Pro Gly Ala Pro Gly Ser Lys Gly Asp Thr Gly Ala Lys  
 435 440 445  
 Gly Glu Pro Gly Pro Val Gly Val Gln Gly Pro Pro Gly Pro Ala Gly  
 450 455 460  
 Glu Glu Gly Lys Arg Gly Ala Arg Gly Glu Pro Gly Pro Thr Gly Leu  
 465 470 475 480  
 Pro Gly Pro Pro Gly Glu Arg Gly Gly Pro Gly Ser Arg Gly Phe Pro  
 485 490 495  
 Gly Ala Asp Gly Val Ala Gly Pro Lys Gly Pro Ala Gly Glu Arg Gly  
 500 505 510  
 Ser Pro Gly Pro Ala Gly Pro Lys Gly Ser Pro Gly Glu Ala Gly Arg  
 515 520 525  
 Pro Gly Glu Ala Gly Leu Pro Gly Ala Lys Gly Leu Thr Gly Ser Pro  
 530 535 540  
 Gly Ser Pro Gly Pro Asp Gly Lys Thr Gly Pro Pro Gly Pro Ala Gly  
 545 550 555 560  
 Gln Asp Gly Arg Pro Gly Pro Pro Gly Pro Pro Gly Ala Arg Gly Gln  
 565 570 575  
 Ala Gly Val Met Gly Phe Pro Gly Pro Lys Gly Ala Ala Gly Glu Pro  
 580 585 590  
 Gly Lys Ala Gly Glu Arg Gly Val Pro Gly Pro Pro Gly Ala Val Gly  
 595 600 605  
 Pro Ala Gly Lys Asp Gly Glu Ala Gly Ala Gln Gly Pro Pro Gly Pro  
 610 615 620  
 Ala Gly Pro Ala Gly Glu Arg Gly Glu Gln Gly Pro Ala Gly Ser Pro  
 625 630 635 640  
 Gly Phe Gln Gly Leu Pro Gly Pro Ala Gly Pro Pro Gly Glu Ala Gly  
 645 650 655  
 Lys Pro Gly Glu Gln Gly Val Pro Gly Asp Leu Gly Ala Pro Gly Pro  
 660 665 670  
 Ser Gly Ala Arg Gly Glu Arg Gly Phe Pro Gly Glu Arg Gly Val Gln  
 675 680 685  
 Gly Pro Pro Gly Pro Ala Gly Pro Arg Gly Ala Asn Gly Ala Pro Gly  
 690 695 700  
 Asn Asp Gly Ala Lys Gly Asp Ala Gly Ala Pro Gly Ala Pro Gly Ser  
 705 710 715 720  
 Gln Gly Ala Pro Gly Leu Gln Gly Met Pro Gly Glu Arg Gly Ala Ala  
 725 730 735  
 Gly Leu Pro Gly Pro Lys Gly Asp Arg Gly Asp Ala Gly Pro Lys Gly  
 740 745 750  
 Ala Asp Gly Ser Pro Gly Lys Asp Gly Val Arg Gly Leu Thr Gly Pro  
 755 760 765  
 Ile Gly Pro Pro Gly Pro Ala Gly Ala Pro Gly Asp Lys Gly Glu Ser  
 770 775 780  
 Gly Pro Ser Gly Pro Ala Gly Pro Thr Gly Ala Arg Gly Ala Pro Gly  
 785 790 795 800  
 Asp Arg Gly Glu Pro Gly Pro Pro Gly Pro Ala Gly Phe Ala Gly Pro  
 805 810 815  
 Pro Gly Ala Asp Gly Gln Pro Gly Ala Lys Gly Glu Pro Gly Asp Ala  
 820 825 830  
 Gly Ala Lys Gly Asp Ala Gly Pro Gly Pro Ala Gly Pro Ala Gly  
 835 840 845  
 Pro Pro Gly Pro Ile Gly Asn Val Gly Ala Pro Gly Ala Lys Gly Ala  
 850 855 860  
 Arg Gly Ser Ala Gly Pro Pro Gly Ala Thr Gly Phe Pro Gly Ala Ala  
 865 870 875 880  
 Gly Arg Val Gly Pro Gly Pro Ser Gly Asn Ala Gly Pro Pro Gly  
 885 890 895



Pro Pro Gly Pro Ala Gly Lys Glu Gly Gly Lys Gly Pro Arg Gly Glu  
 900 905 910  
 Thr Gly Pro Ala Gly Arg Pro Gly Glu Val Gly Pro Pro Gly Pro Pro  
 915 920 925  
 Gly Pro Ala Gly Glu Lys Gly Ser Pro Gly Ala Asp Gly Pro Ala Gly  
 930 935 940  
 Ala Pro Gly Thr Pro Gly Pro Gln Gly Ile Ala Gly Gln Arg Gly Val  
 945 950 955 960  
 Val Gly Leu Pro Gly Gln Arg Gly Glu Arg Gly Phe Pro Gly Leu Pro  
 965 970 975  
 Gly Pro Ser Gly Glu Pro Gly Lys Gln Gly Pro Ser Gly Ala Ser Gly  
 980 985 990  
 Glu Arg Gly Pro Pro Gly Pro Met Gly Pro Pro Gly Leu Ala Gly Pro  
 995 1000 1005  
 Pro Gly Glu Ser Gly Arg Glu Gly Ala Pro Ala Ala Glu Gly Ser  
 1010 1015 1020  
 Pro Gly Arg Asp Gly Ser Pro Gly Ala Lys Gly Asp Arg Gly Glu  
 1025 1030 1035  
 Thr Gly Pro Ala Gly Pro Pro Gly Ala Pro Gly Ala Pro Gly Ala  
 1040 1045 1050  
 Pro Gly Pro Val Gly Pro Ala Gly Lys Ser Gly Asp Arg Gly Glu  
 1055 1060 1065  
 Thr Gly Pro Ala Gly Pro Ala Gly Pro Val Gly Pro Val Gly Ala  
 1070 1075 1080  
 Arg Gly Pro Ala Gly Pro Gln Gly Pro Arg Gly Asp Lys Gly Glu  
 1085 1090 1095  
 Thr Gly Glu Gln Gly Asp Arg Gly Ile Lys Gly His Arg Gly Phe  
 1100 1105 1110  
 Ser Gly Leu Gln Gly Pro Pro Gly Pro Pro Gly Ser Pro Gly Glu  
 1115 1120 1125  
 Gln Gly Pro Ser Gly Ala Ser Gly Pro Ala Gly Pro Arg Gly Pro  
 1130 1135 1140  
 Pro Gly Ser Ala Gly Ala Pro Gly Lys Asp Gly Leu Asn Gly Leu  
 1145 1150 1155  
 Pro Gly Pro Ile Gly Pro Pro Gly Pro Arg Gly Arg Thr Gly Asp  
 1160 1165 1170  
 Ala Gly Pro Val Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly Pro  
 1175 1180 1185  
 Pro Gly Pro Pro Ser Ala Gly Phe Asp Phe Ser Phe Leu Pro Gln  
 1190 1195 1200  
 Pro Pro Gln Glu Lys Ala His Asp Gly Gly Arg Tyr Tyr Arg Ala  
 1205 1210 1215  
 Asp Asp Ala Asn Val Val Arg Asp Arg Asp Leu Glu Val Asp Thr  
 1220 1225 1230  
 Thr Leu Lys Ser Leu Ser Gln Ile Glu Asn Ile Arg Ser Pro  
 1235 1240 1245  
 Glu Gly Ser Arg Lys Asn Pro Ala Arg Thr Cys Arg Asp Leu Lys  
 1250 1255 1260  
 Met Cys His Ser Asp Trp Lys Ser Gly Glu Tyr Trp Ile Asp Pro  
 1265 1270 1275  
 Asn Gln Gly Cys Asn Leu Asp Ala Ile Lys Val Phe Cys Asn Met  
 1280 1285 1290  
 Glu Thr Gly Glu Thr Cys Val Tyr Pro Thr Gln Pro Ser Val Ala  
 1295 1300 1305  
 Gln Lys Asn Trp Tyr Ile Ser Lys Asn Pro Lys Asp Lys Arg His  
 1310 1315 1320  
 Val Trp Phe Gly Glu Ser Met Thr Asp Gly Phe Gln Phe Glu Tyr  
 1325 1330 1335  
 Gly Gly Gln Gly Ser Asp Pro Ala Asp Val Ala Ile Gln Leu Thr  
 1340 1345 1350  
 Phe Leu Arg Leu Met Ser Thr Glu Ala Ser Gln Asn Ile Thr Tyr  
 1355 1360 1365

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His Cys Lys Asn Ser Val Ala Tyr Met Asp Gln Gln Thr Gly Asn  
 1370 1375 1380  
 Leu Lys Lys Ala Leu Leu Leu Lys Gly Ser Asn Glu Ile Glu Ile  
 1385 1390 1395  
 Arg Ala Glu Gly Asn Ser Arg Phe Thr Tyr Ser Val Thr Val Asp  
 1400 1405 1410  
 Gly Cys Thr Ser His Thr Gly Ala Trp Gly Lys Thr Val Ile Glu  
 1415 1420 1425  
 Tyr Lys Thr Thr Lys Ser Ser Arg Leu Pro Ile Ile Asp Val Ala  
 1430 1435 1440  
 Pro Leu Asp Val Gly Ala Pro Asp Gln Glu Phe Gly Phe Asp Val  
 1445 1450 1455  
 Gly Pro Val Cys Phe Leu  
 1460

&lt;210&gt; 319

&lt;211&gt; 764

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 319  
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 Gly Leu Leu Ser Gly Gly Val Thr Thr Thr Pro Trp Ser Leu Ala Gln  
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 Pro Gln Gly Ser Cys Ser Leu Glu Gly Val Glu Ile Lys Gly Gly Ser  
 35 40 45  
 Phe Arg Leu Leu Gln Glu Gly Gln Ala Leu Glu Tyr Thr Val Cys Pro Ser  
 50 55 60  
 Gly Phe Tyr Pro Tyr Pro Val Gln Thr Arg Thr Cys Arg Ser Thr Gly  
 65 70 75 80  
 Ser Trp Ser Thr Leu Lys Thr Gln Asp Gln Lys Thr Val Arg Lys Ala  
 85 90 95  
 Glu Cys Arg Ala Ile His Cys Pro Arg Pro His Asp Phe Glu Asn Gly  
 100 105 110  
 Glu Tyr Trp Pro Arg Ser Pro Tyr Tyr Asn Val Ser Asp Glu Ile Ser  
 115 120 125  
 Phe His Cys Tyr Asp Gly Tyr Thr Leu Arg Gly Ser Ala Asn Arg Thr  
 130 135 140  
 Cys Gln Val Asn Gly Arg Trp Ser Gly Gln Thr Ala Ile Cys Asp Asn  
 145 150 155 160  
 Gly Ala Gly Tyr Cys Ser Asn Pro Gly Ile Pro Ile Gly Thr Arg Lys  
 165 170 175  
 Val Gly Ser Gln Tyr Arg Leu Glu Asp Ser Val Thr Tyr His Cys Ser  
 180 185 190  
 Arg Gly Leu Thr Leu Arg Gly Ser Gln Arg Arg Thr Cys Gln Glu Gly  
 195 200 205  
 Gly Ser Trp Ser Gly Thr Glu Pro Ser Cys Gln Asp Ser Phe Met Tyr  
 210 215 220  
 Asp Thr Pro Gln Glu Val Ala Glu Ala Phe Leu Ser Ser Leu Thr Glu  
 225 230 235 240  
 Thr Ile Glu Gly Val Asp Ala Glu Asp Gly His Gly Pro Gly Glu Gln  
 245 250 255  
 Gln Lys Arg Lys Ile Val Leu Asp Pro Ser Gly Ser Met Asn Ile Tyr  
 260 265 270  
 Leu Val Leu Asp Gly Ser Asp Ser Ile Gly Ala Ser Asn Phe Thr Gly  
 275 280 285

Ala Lys Lys Cys Leu Val Asn Leu Ile Glu Lys Val Ala Ser Tyr Gly  
 290 295 300  
 Val Lys Pro Arg Tyr Gly Leu Val Thr Tyr Ala Thr Tyr Pro Lys Ile  
 305 310 315 320  
 Trp Val Lys Val Ser Glu Ala Asp Ser Ser Asn Ala Asp Trp Val Thr  
 325 330 335  
 Lys Gln Leu Asn Glu Ile Asn Tyr Glu Asp His Lys Leu Lys Ser Gly  
 340 345 350  
 Thr Asn Thr Lys Lys Ala Leu Gln Ala Val Tyr Ser Met Met Ser Trp  
 355 360 365  
 Pro Asp Asp Val Pro Pro Glu Gly Trp Asn Arg Thr Arg His Val Ile  
 370 375 380  
 Ile Leu Met Thr Asp Gly Leu His Asn Met Gly Gly Asp Pro Ile Thr  
 385 390 395 400  
 Val Ile Asp Glu Ile Arg Asp Leu Leu Tyr Ile Gly Lys Asp Arg Lys  
 405 410 415  
 Asn Pro Arg Glu Asp Tyr Leu Asp Val Tyr Val Phe Gly Val Gly Pro  
 420 425 430  
 Leu Val Asn Gln Val Asn Ile Asn Ala Leu Ala Ser Lys Lys Asp Asn  
 435 440 445  
 Glu Gln His Val Phe Lys Val Lys Asp Met Glu Asn Leu Glu Asp Val  
 450 455 460  
 Phe Tyr Gln Met Ile Asp Glu Ser Gln Ser Leu Ser Leu Cys Gly Met  
 465 470 475 480  
 Val Trp Glu His Arg Lys Gly Thr Asp Tyr His Lys Gln Pro Trp Gln  
 485 490 495  
 Ala Lys Ile Ser Val Ile Arg Pro Ser Lys Gly His Glu Ser Cys Met  
 500 505 510  
 Gly Ala Val Val Ser Glu Tyr Phe Val Leu Thr Ala Ala His Cys Phe  
 515 520 525  
 Thr Val Asp Asp Lys Glu His Ser Ile Lys Val Ser Val Gly Gly Glu  
 530 535 540  
 Lys Arg Asp Leu Glu Ile Glu Val Val Leu Phe His Pro Asn Tyr Asn  
 545 550 555 560  
 Ile Asn Gly Lys Lys Glu Ala Gly Ile Pro Glu Phe Tyr Asp Tyr Asp  
 565 570 575  
 Val Ala Leu Ile Lys Leu Lys Asn Lys Leu Lys Tyr Gly Gln Thr Ile  
 580 585 590  
 Arg Pro Ile Cys Leu Pro Cys Thr Glu Gly Thr Thr Arg Ala Leu Arg  
 595 600 605  
 Leu Pro Pro Thr Thr Thr Cys Gln Gln Gln Lys Glu Glu Leu Leu Pro  
 610 615 620  
 Ala Gln Asp Ile Lys Ala Leu Phe Val Ser Glu Glu Glu Lys Lys Leu  
 625 630 635 640  
 Thr Arg Lys Glu Val Tyr Ile Lys Asn Gly Asp Lys Lys Gly Ser Cys  
 645 650 655  
 Glu Arg Asp Ala Gln Tyr Ala Pro Gly Tyr Asp Lys Val Lys Asp Ile  
 660 665 670  
 Ser Glu Val Val Thr Pro Arg Phe Leu Cys Thr Gly Gly Val Ser Pro  
 675 680 685  
 Tyr Ala Asp Pro Asn Thr Cys Arg Gly Asp Ser Gly Gly Pro Leu Ile  
 690 695 700  
 Val His Lys Arg Ser Arg Phe Ile Gln Val Gly Val Ile Ser Trp Gly  
 705 710 715 720  
 Val Val Asp Val Cys Lys Asn Gln Lys Arg Gln Lys Gln Val Pro Ala  
 725 730 735  
 His Ala Arg Asp Phe His Ile Asn Leu Phe Gln Val Leu Pro Trp Leu  
 740 745 750  
 Lys Glu Lys Leu Gln Asp Glu Asp Leu Gly Phe Leu  
 755 760

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&lt;210&gt; 320

&lt;211&gt; 909

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 320

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Met Ala Ala Arg Pro Leu Pro Val Ser Pro Ala Arg Ala Leu Leu Leu
1      5      10      15
Ala Leu Ala Gly Ala Leu Leu Ala Pro Cys Glu Ala Arg Gly Val Ser
20      25      30
Leu Trp Asn Gln Gly Arg Ala Asp Glu Val Val Ser Ala Ser Val Arg
35      40      45
Ser Gly Asp Leu Trp Ile Pro Val Lys Ser Phe Asp Ser Lys Asn His
50      55      60
Pro Glu Val Leu Asn Ile Arg Leu Gln Arg Glu Ser Lys Glu Leu Ile
65      70      75      80
Ile Asn Leu Glu Arg Asn Glu Gly Leu Ile Ala Ser Ser Phe Thr Glu
85      90      95
Thr His Tyr Leu Gln Asp Gly Thr Asp Val Ser Leu Ala Arg Asn Tyr
100      105      110
Thr Val Ile Leu Gly His Cys Tyr Tyr His Gly His Val Arg Gly Tyr
115      120      125
Ser Asp Ser Ala Val Ser Leu Ser Thr Cys Ser Gly Leu Arg Gly Leu
130      135      140
Ile Val Phe Glu Asn Glu Ser Tyr Val Leu Glu Pro Met Lys Ser Ala
145      150      155      160
Thr Asn Arg Tyr Lys Leu Phe Pro Ala Lys Lys Leu Lys Ser Val Arg
165      170      175
Gly Ser Cys Gly Ser His His Asn Thr Pro Asn Leu Ala Ala Lys Asn
180      185      190
Val Phe Pro Pro Pro Ser Gln Thr Trp Ala Arg Arg His Lys Arg Glu
195      200      205
Thr Leu Lys Ala Thr Lys Tyr Val Glu Leu Val Ile Val Ala Asp Asn
210      215      220
Arg Glu Phe Gln Arg Gln Gly Lys Asp Leu Glu Lys Val Lys Gln Arg
225      230      235      240
Leu Ile Glu Ile Ala Asn His Val Asp Lys Phe Tyr Arg Pro Leu Asn
245      250      255
Ile Arg Ile Val Leu Val Gly Val Glu Val Trp Asn Asp Met Asp Lys
260      265      270
Cys Ser Val Ser Gln Asp Pro Phe Thr Ser Leu His Glu Phe Leu Asp
275      280      285
Trp Arg Lys Met Lys Leu Leu Pro Arg Lys Ser His Asp Asn Ala Gln
290      295      300
Leu Val Ser Gly Val Tyr Phe Gln Gly Thr Thr Ile Gly Met Ala Pro
305      310      315      320
Ile Met Ser Met Cys Thr Ala Asp Gln Ser Gly Gly Ile Val Met Asp
325      330      335
His Ser Asp Asn Pro Leu Gly Ala Ala Val Thr Leu Ala His Glu Leu
340      345      350
Gly His Asn Phe Gly Met Asn His Asp Thr Leu Asp Arg Gly Cys Ser
355      360      365
Cys Gln Met Ala Val Glu Lys Gly Gly Cys Ile Met Asn Ala Ser Thr
370      375      380
Gly Tyr Pro Phe Pro Met Val Phe Ser Ser Cys Ser Arg Lys Asp Leu
385      390      395      400

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Glu	Thr	Ser	Leu	Glu	Lys	Gly	Met	Gly	Val	Cys	Leu	Phe	Asn	Leu	Pro
				405					410					415	
Glu	Val	Arg	Glu	Ser	Phe	Gly	Gly	Gln	Lys	Cys	Gly	Asn	Arg	Phe	Val
			420					425					430		
Glu	Glu	Gly	Glu	Glu	Cys	Asp	Cys	Gly	Glu	Pro	Glu	Glu	Cys	Met	Asn
		435					440					445			
Arg	Cys	Cys	Asn	Ala	Thr	Thr	Cys	Thr	Leu	Lys	Pro	Asp	Ala	Val	Cys
	450					455					460				
Ala	His	Gly	Leu	Cys	Cys	Glu	Asp	Cys	Gln	Leu	Lys	Pro	Ala	Gly	Thr
465					470					475					480
Ala	Cys	Arg	Asp	Ser	Ser	Asn	Ser	Cys	Asp	Leu	Pro	Glu	Phe	Cys	Thr
			485						490					495	
Gly	Ala	Ser	Pro	His	Cys	Pro	Ala	Asn	Val	Tyr	Leu	His	Asp	Gly	His
			500					505					510		
Ser	Cys	Gln	Asp	Val	Asp	Gly	Tyr	Cys	Tyr	Asn	Gly	Ile	Cys	Gln	Thr
		515					520					525			
His	Glu	Gln	Gln	Cys	Val	Thr	Leu	Trp	Gly	Pro	Gly	Ala	Lys	Pro	Ala
	530					535					540				
Pro	Gly	Ile	Cys	Phe	Glu	Arg	Val	Asn	Ser	Ala	Gly	Asp	Pro	Tyr	Gly
545					550					555					560
Asn	Cys	Gly	Lys	Val	Ser	Lys	Ser	Ser	Phe	Ala	Lys	Cys	Glu	Met	Arg
				565					570					575	
Asp	Ala	Lys	Cys	Gly	Lys	Ile	Gln	Cys	Gln	Gly	Gly	Ala	Ser	Arg	Pro
			580				585						590		
Val	Ile	Gly	Thr	Asn	Ala	Val	Ser	Ile	Glu	Thr	Asn	Ile	Pro	Leu	Gln
		595					600					605			
Gln	Gly	Gly	Arg	Ile	Leu	Cys	Arg	Gly	Thr	His	Val	Tyr	Leu	Gly	Asp
	610					615					620				
Asp	Met	Pro	Asp	Pro	Gly	Leu	Val	Leu	Ala	Gly	Thr	Lys	Cys	Ala	Asp
625					630					635					640
Gly	Lys	Ile	Cys	Leu	Asn	Arg	Gln	Cys	Gln	Asn	Ile	Ser	Val	Phe	Gly
				645					650					655	
Val	His	Glu	Cys	Ala	Met	Gln	Cys	His	Gly	Arg	Gly	Val	Cys	Asn	Asn
			660					665					670		
Arg	Lys	Asn	Cys	His	Cys	Glu	Ala	His	Trp	Ala	Pro	Pro	Phe	Cys	Asp
		675					680						685		
Lys	Phe	Gly	Phe	Gly	Gly	Ser	Thr	Asp	Ser	Gly	Pro	Ile	Arg	Gln	Ala
	690					695					700				
Asp	Asn	Gln	Gly	Leu	Thr	Ile	Gly	Ile	Leu	Val	Thr	Ile	Leu	Cys	Leu
705					710					715					720
Leu	Ala	Ala	Gly	Phe	Val	Val	Tyr	Leu	Lys	Arg	Lys	Thr	Leu	Ile	Arg
			725						730					735	
Leu	Leu	Phe	Thr	Asn	Lys	Lys	Thr	Thr	Ile	Glu	Lys	Leu	Arg	Cys	Val
			740					745					750		
Arg	Pro	Ser	Arg	Pro	Pro	Arg	Gly	Phe	Gln	Pro	Cys	Gln	Ala	His	Leu
		755					760						765		
Gly	His	Leu	Gly	Lys	Gly	Leu	Met	Arg	Lys	Pro	Pro	Asp	Ser	Tyr	Pro
	770					775					780				
Pro	Lys	Asp	Asn	Pro	Arg	Arg	Leu	Leu	Gln	Cys	Gln	Asn	Val	Asp	Ile
785					790					795					800
Ser	Arg	Pro	Leu	Asn	Gly	Leu	Asn	Val	Pro	Gln	Pro	Gln	Ser	Thr	Gln
			805						810					815	
Arg	Val	Leu	Pro	Pro	Leu	His	Arg	Ala	Pro	Arg	Ala	Pro	Ser	Val	Pro
			820					825					830		
Ala	Arg	Pro	Leu	Pro	Ala	Lys	Pro	Ala	Leu	Arg	Gln	Ala	Gln	Gly	Thr
		835					840					845			
Cys	Lys	Pro	Asn	Pro	Pro	Gln	Lys	Pro	Leu	Pro	Ala	Asp	Pro	Leu	Ala
	850					855					860				
Arg	Thr	Thr	Arg	Leu	Thr	His	Ala	Leu	Ala	Arg	Thr	Pro	Gly	Gln	Trp
865					870					875					880

Glu Thr Gly Leu Arg Leu Ala Pro Leu Arg Pro Ala Pro Gln Tyr Pro  
 885 890 895  
 His Gln Val Pro Arg Ser Thr His Thr Ala Tyr Ile Lys  
 900 905

<210> 321

<211> 574

<212> PRT

<213> Homo sapiens

<400> 321

Met Ala Leu Ala Arg Gly Ser Arg Gln Leu Gly Ala Leu Val Trp Gly  
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 Ala Cys Leu Cys Val Leu Val His Gly Gln Gln Ala Gln Pro Gly Gln  
 20 25 30  
 Gly Ser Asp Pro Ala Arg Trp Arg Gln Leu Ile Gln Trp Glu Asn Asn  
 35 40 45  
 Gly Gln Val Tyr Ser Leu Leu Asn Ser Gly Ser Glu Tyr Val Pro Ala  
 50 55 60  
 Gly Pro Gln Arg Ser Glu Ser Ser Ser Arg Val Leu Leu Ala Gly Ala  
 65 70 75 80  
 Pro Gln Ala Gln Gln Arg Arg Ser His Gly Ser Pro Arg Arg Arg Gln  
 85 90 95  
 Ala Pro Ser Leu Pro Leu Pro Gly Arg Val Gly Ser Asp Thr Val Arg  
 100 105 110  
 Gly Gln Ala Arg His Pro Phe Gly Phe Gly Gln Val Pro Asp Asn Trp  
 115 120 125  
 Arg Glu Val Ala Val Gly Asp Ser Thr Gly Met Ala Leu Ala Arg Thr  
 130 135 140  
 Ser Val Ser Gln Gln Arg His Gly Gly Ser Ala Ser Ser Val Ser Ala  
 145 150 155 160  
 Ser Ala Phe Ala Ser Thr Tyr Arg Gln Gln Pro Ser Tyr Pro Gln Gln  
 165 170 175  
 Phe Pro Tyr Pro Gln Ala Pro Phe Val Ser Gln Tyr Glu Asn Tyr Asp  
 180 185 190  
 Pro Ala Ser Arg Thr Tyr Asp Gln Gly Phe Val Tyr Tyr Arg Pro Ala  
 195 200 205  
 Gly Gly Gly Val Gly Ala Gly Ala Ala Val Ala Ser Ala Gly Val  
 210 215 220  
 Ile Tyr Pro Tyr Gln Pro Arg Ala Arg Tyr Glu Glu Tyr Gly Gly Gly  
 225 230 235 240  
 Glu Glu Leu Pro Glu Tyr Pro Pro Gln Gly Phe Tyr Pro Ala Pro Glu  
 245 250 255  
 Arg Pro Tyr Val Pro Pro Pro Pro Pro Pro Asp Gly Leu Asp Arg  
 260 265 270  
 Arg Tyr Ser His Ser Leu Tyr Ser Glu Gly Thr Pro Gly Phe Glu Gln  
 275 280 285  
 Ala Tyr Pro Asp Pro Gly Pro Glu Ala Ala Gln Ala His Gly Gly Asp  
 290 295 300  
 Pro Arg Leu Gly Trp Tyr Pro Pro Tyr Ala Asn Pro Pro Pro Glu Ala  
 305 310 315 320  
 Tyr Gly Pro Pro Arg Ala Leu Glu Pro Pro Tyr Leu Pro Val Arg Ser  
 325 330 335  
 Ser Asp Thr Pro Pro Gly Gly Glu Arg Asn Gly Ala Gln Gln Gly  
 340 345 350  
 Arg Leu Ser Val Gly Ser Val Tyr Arg Pro Asn Gln Asn Gly Arg Gly  
 355 360 365

Leu Pro Asp Leu Val Pro Asp Pro Asn Tyr Val Gln Ala Ser Thr Tyr  
 370 375 380  
 Val Gln Arg Ala His Leu Tyr Ser Leu Arg Cys Ala Ala Glu Glu Lys  
 385 390 395 400  
 Cys Leu Ala Ser Thr Ala Tyr Ala Pro Glu Ala Thr Asp Tyr Asp Val  
 405 410 415  
 Arg Val Leu Leu Arg Phe Pro Gln Arg Val Lys Asn Gln Gly Thr Ala  
 420 425 430  
 Asp Phe Leu Pro Asn Arg Pro Arg His Thr Trp Glu Trp His Ser Cys  
 435 440 445  
 His Gln His Tyr His Ser Met Asp Glu Phe Ser His Tyr Asp Leu Leu  
 450 455 460  
 Asp Ala Ala Thr Gly Lys Lys Val Ala Glu Gly His Lys Ala Ser Phe  
 465 470 475 480  
 Cys Leu Glu Asp Ser Thr Cys Asp Phe Gly Asn Leu Lys Arg Tyr Ala  
 485 490 495  
 Cys Thr Ser His Thr Gln Gly Leu Ser Pro Gly Cys Tyr Asp Thr Tyr  
 500 505 510  
 Asn Ala Asp Ile Asp Cys Gln Trp Ile Asp Ile Thr Asp Val Gln Pro  
 515 520 525  
 Gly Asn Tyr Ile Leu Lys Val His Val Asn Pro Lys Tyr Ile Val Leu  
 530 535 540  
 Glu Ser Asp Phe Thr Asn Asn Val Val Arg Cys Asn Ile His Tyr Thr  
 545 550 555 560  
 Gly Arg Tyr Val Ser Ala Thr Asn Cys Lys Ile Val Gln Ser  
 565 570

&lt;210&gt; 322

&lt;211&gt; 344

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 322  
 Met Gly Pro Pro Ser Ala Pro Pro Cys Arg Leu His Val Pro Trp Lys  
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 Glu Val Leu Leu Thr Ala Ser Leu Leu Thr Phe Trp Asn Pro Pro Thr  
 20 25 30  
 Thr Ala Lys Leu Thr Ile Glu Ser Thr Pro Phe Asn Val Ala Glu Gly  
 35 40 45  
 Lys Glu Val Leu Leu Leu Ala His Asn Leu Pro Gln Asn Arg Ile Gly  
 50 55 60  
 Tyr Ser Trp Tyr Lys Gly Glu Arg Val Asp Gly Asn Ser Leu Ile Val  
 65 70 75 80  
 Gly Tyr Val Ile Gly Thr Gln Gln Ala Thr Pro Gly Pro Ala Tyr Ser  
 85 90 95  
 Gly Arg Glu Thr Ile Tyr Pro Asn Ala Ser Leu Leu Ile Gln Asn Val  
 100 105 110  
 Thr Gln Asn Asp Thr Gly Phe Tyr Thr Leu Gln Val Ile Lys Ser Asp  
 115 120 125  
 Leu Val Asn Glu Glu Ala Thr Gly Gln Phe His Val Tyr Pro Glu Leu  
 130 135 140  
 Pro Lys Pro Ser Ile Ser Ser Asn Asn Ser Asn Pro Val Glu Asp Lys  
 145 150 155 160  
 Asp Ala Val Ala Phe Thr Cys Glu Pro Glu Val Gln Asn Thr Thr Tyr  
 165 170 175  
 Leu Trp Trp Val Asn Gly Gln Ser Leu Pro Val Ser Pro Arg Leu Gln  
 180 185 190

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Leu Ser Asn Gly Asn Met Thr Leu Thr Leu Leu Ser Val Lys Arg Asn  
 195 200 205  
 Asp Ala Gly Ser Tyr Glu Cys Glu Ile Gln Asn Pro Ala Ser Ala Asn  
 210 215 220  
 Arg Ser Asp Pro Val Thr Leu Asn Val Leu Tyr Gly Pro Asp Val Pro  
 225 230 235 240  
 Thr Ile Ser Pro Ser Lys Ala Asn Tyr Arg Pro Gly Glu Asn Leu Asn  
 245 250 255  
 Leu Ser Cys His Ala Ala Ser Asn Pro Pro Ala Gln Tyr Ser Trp Phe  
 260 265 270  
 Ile Asn Gly Thr Phe Gln Gln Ser Thr Gln Glu Leu Phe Ile Pro Asn  
 275 280 285  
 Ile Thr Val Asn Asn Ser Gly Ser Tyr Met Cys Gln Ala His Asn Ser  
 290 295 300  
 Ala Thr Gly Leu Asn Arg Thr Thr Val Thr Met Ile Thr Val Ser Gly  
 305 310 315 320  
 Ser Ala Pro Val Leu Ser Ala Val Ala Thr Val Gly Ile Thr Ile Gly  
 325 330 335  
 Val Leu Ala Arg Val Ala Leu Ile  
 340

&lt;210&gt; 323

&lt;211&gt; 488

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 323  
 Met Ala Pro Ala Ala Trp Leu Arg Ser Ala Ala Ala Arg Ala Leu Leu  
 1 5 10 15  
 Pro Pro Met Leu Leu Leu Leu Leu Gln Pro Pro Pro Leu Leu Ala Arg  
 20 25 30  
 Ala Leu Pro Pro Asp Val His His Leu His Ala Glu Arg Arg Gly Pro  
 35 40 45  
 Gln Pro Trp His Ala Ala Leu Pro Ser Ser Pro Ala Pro Ala Pro Ala  
 50 55 60  
 Thr Gln Glu Ala Pro Arg Pro Ala Ser Ser Leu Arg Pro Pro Arg Cys  
 65 70 75 80  
 Gly Val Pro Asp Pro Ser Asp Gly Leu Ser Ala Arg Asn Arg Gln Lys  
 85 90 95  
 Arg Phe Val Leu Ser Gly Gly Arg Trp Glu Lys Thr Asp Leu Thr Tyr  
 100 105 110  
 Arg Ile Leu Arg Phe Pro Trp Gln Leu Val Gln Glu Gln Val Arg Gln  
 115 120 125  
 Thr Met Ala Glu Ala Leu Lys Val Trp Ser Asp Val Thr Pro Leu Thr  
 130 135 140  
 Phe Thr Glu Val His Glu Gly Arg Ala Asp Ile Met Ile Asp Phe Ala  
 145 150 155 160  
 Arg Tyr Trp His Gly Asp Asp Leu Pro Phe Asp Gly Pro Gly Gly Ile  
 165 170 175  
 Leu Ala His Ala Phe Phe Pro Lys Thr His Arg Glu Gly Asp Val His  
 180 185 190  
 Phe Asp Tyr Asp Glu Thr Trp Thr Ile Gly Asp Asp Gln Gly Thr Asp  
 195 200 205  
 Leu Leu Gln Val Ala Ala His Glu Phe Gly His Val Leu Gly Leu Gln  
 210 215 220  
 His Thr Thr Ala Ala Lys Ala Leu Met Ser Ala Phe Tyr Thr Phe Arg  
 225 230 235 240



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Tyr Pro Leu Ser Leu Ser Pro Asp Asp Cys Arg Gly Val Gln His Leu  
 245 250 255  
 Tyr Gly Gln Pro Trp Pro Thr Val Thr Ser Arg Thr Pro Ala Leu Gly  
 260 265 270  
 Pro Gln Ala Gly Ile Asp Thr Asn Glu Ile Ala Pro Leu Glu Pro Asp  
 275 280 285  
 Ala Pro Pro Asp Ala Cys Glu Ala Ser Phe Asp Ala Val Ser Thr Ile  
 290 295 300  
 Arg Gly Glu Leu Phe Phe Phe Lys Ala Gly Phe Val Trp Arg Leu Arg  
 305 310 315 320  
 Gly Gly Gln Leu Gln Pro Gly Tyr Pro Ala Leu Ala Ser Arg His Trp  
 325 330 335  
 Gln Gly Leu Pro Ser Pro Val Asp Ala Ala Phe Glu Asp Ala Gln Gly  
 340 345 350  
 His Ile Trp Phe Phe Gln Gly Ala Gln Tyr Trp Val Tyr Asp Gly Glu  
 355 360 365  
 Lys Pro Val Leu Gly Pro Ala Pro Leu Thr Glu Leu Gly Leu Val Arg  
 370 375 380  
 Phe Pro Val His Ala Ala Leu Val Trp Gly Pro Glu Lys Asn Lys Ile  
 385 390 395 400  
 Tyr Phe Phe Arg Gly Arg Asp Tyr Trp Arg Phe His Pro Ser Thr Arg  
 405 410 415  
 Arg Val Asp Ser Pro Val Pro Arg Arg Ala Thr Asp Trp Arg Gly Val  
 420 425 430  
 Pro Ser Glu Ile Asp Ala Ala Phe Gln Asp Ala Asp Gly Tyr Ala Tyr  
 435 440 445  
 Phe Leu Arg Gly Arg Leu Tyr Trp Lys Phe Asp Pro Val Lys Val Lys  
 450 455 460  
 Ala Leu Glu Gly Phe Pro Arg Leu Val Gly Pro Asp Phe Phe Gly Cys  
 465 470 475 480  
 Ala Glu Pro Ala Asn Thr Phe Leu  
 485

&lt;210&gt; 324

&lt;211&gt; 469

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 324

Met His Ser Phe Pro Pro Leu Leu Leu Leu Leu Phe Trp Gly Val Val  
 1 5 10 15  
 Ser His Ser Phe Pro Ala Thr Leu Glu Thr Gln Glu Gln Asp Val Asp  
 20 25 30  
 Leu Val Gln Lys Tyr Leu Glu Lys Tyr Tyr Asn Leu Lys Asn Asp Gly  
 35 40 45  
 Arg Gln Val Glu Lys Arg Arg Asn Ser Gly Pro Val Val Glu Lys Leu  
 50 55 60  
 Lys Gln Met Gln Glu Phe Phe Gly Leu Lys Val Thr Gly Lys Pro Asp  
 65 70 75 80  
 Ala Glu Thr Leu Lys Val Met Lys Gln Pro Arg Cys Gly Val Pro Asp  
 85 90 95  
 Val Ala Gln Phe Val Leu Thr Glu Gly Asn Pro Arg Trp Glu Gln Thr  
 100 105 110  
 His Leu Thr Tyr Arg Ile Glu Asn Tyr Thr Pro Asp Leu Pro Arg Ala  
 115 120 125  
 Asp Val Asp His Ala Ile Glu Lys Ala Phe Gln Leu Trp Ser Asn Val  
 130 135 140

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Thr Pro Leu Thr Phe Thr Lys Val Ser Glu Gly Gln Ala Asp Ile Met  
 145 150 155 160  
 Ile Ser Phe Val Arg Gly Asp His Arg Asp Asn Ser Pro Phe Asp Gly  
 165 170 175  
 Pro Gly Gly Asn Leu Ala His Ala Phe Gln Pro Gly Pro Gly Ile Gly  
 180 185 190  
 Gly Asp Ala His Phe Asp Glu Asp Glu Arg Trp Thr Asn Asn Phe Arg  
 195 200 205  
 Glu Tyr Asn Leu His Arg Val Ala Ala His Glu Leu Gly His Ser Leu  
 210 215 220  
 Gly Leu Ser His Ser Thr Asp Ile Gly Ala Leu Met Tyr Pro Ser Tyr  
 225 230 235 240  
 Thr Phe Ser Gly Asp Val Gln Leu Ala Gln Asp Asp Ile Asp Gly Ile  
 245 250 255  
 Gln Ala Ile Tyr Gly Arg Ser Gln Asn Pro Val Gln Pro Ile Gly Pro  
 260 265 270  
 Gln Thr Pro Lys Ala Cys Asp Ser Lys Leu Thr Phe Asp Ala Ile Thr  
 275 280 285  
 Thr Ile Arg Gly Glu Val Met Phe Phe Lys Asp Arg Phe Tyr Met Arg  
 290 295 300  
 Thr Asn Pro Phe Tyr Pro Glu Val Glu Leu Asn Phe Ile Ser Val Phe  
 305 310 315 320  
 Trp Pro Gln Leu Pro Asn Gly Leu Glu Ala Ala Tyr Glu Phe Ala Asp  
 325 330 335  
 Arg Asp Glu Val Arg Phe Phe Lys Gly Asn Lys Tyr Trp Ala Val Gln  
 340 345 350  
 Gly Gln Asn Val Leu His Gly Tyr Pro Lys Asp Ile Tyr Ser Ser Phe  
 355 360 365  
 Gly Phe Pro Arg Thr Val Lys His Ile Asp Ala Ala Leu Ser Glu Glu  
 370 375 380  
 Asn Thr Gly Lys Thr Tyr Phe Phe Val Ala Asn Lys Tyr Trp Arg Tyr  
 385 390 395 400  
 Asp Glu Tyr Lys Arg Ser Met Asp Pro Gly Tyr Pro Lys Met Ile Ala  
 405 410 415  
 His Asp Phe Pro Gly Ile Gly His Lys Val Asp Ala Val Phe Met Lys  
 420 425 430  
 Asp Gly Phe Phe Tyr Phe Phe His Gly Thr Arg Gln Tyr Lys Phe Asp  
 435 440 445  
 Pro Lys Thr Lys Arg Ile Leu Thr Leu Gln Lys Ala Asn Ser Trp Phe  
 450 455 460  
 Asn Cys Arg Lys Asn  
 465

&lt;210&gt; 325

&lt;211&gt; 471

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 325

Met His Pro Gly Val Leu Ala Ala Phe Leu Phe Leu Ser Trp Thr His  
 1 5 10 15  
 Cys Arg Ala Leu Pro Leu Pro Ser Gly Gly Asp Glu Asp Asp Leu Ser  
 20 25 30  
 Glu Glu Asp Leu Gln Phe Ala Glu Arg Tyr Leu Arg Ser Tyr Tyr His  
 35 40 45  
 Pro Thr Asn Leu Ala Gly Ile Leu Lys Glu Asn Ala Ala Ser Ser Met  
 50 55 60

Thr Glu Arg Leu Arg Glu Met Gln Ser Phe Phe Gly Leu Glu Val Thr  
 65 70 75 80  
 Gly Lys Leu Asp Asp Asn Thr Leu Asp Val Met Lys Lys Pro Arg Cys  
 85 90 95  
 Gly Val Pro Asp Val Gly Glu Tyr Asn Val Phe Pro Arg Thr Leu Lys  
 100 105 110  
 Trp Ser Lys Met Asn Leu Thr Tyr Arg Ile Val Asn Tyr Thr Pro Asp  
 115 120 125  
 Met Thr His Ser Glu Val Glu Lys Ala Phe Lys Lys Ala Phe Lys Val  
 130 135 140  
 Trp Ser Asp Val Thr Pro Leu Asn Phe Thr Arg Leu His Asp Gly Ile  
 145 150 155 160  
 Ala Asp Ile Met Ile Ser Phe Gly Ile Lys Glu His Gly Asp Phe Tyr  
 165 170 175  
 Pro Phe Asp Gly Pro Ser Gly Leu Leu Ala His Ala Phe Pro Pro Gly  
 180 185 190  
 Pro Asn Tyr Gly Gly Asp Ala His Phe Asp Asp Asp Glu Thr Trp Thr  
 195 200 205  
 Ser Ser Ser Lys Gly Tyr Asn Leu Phe Leu Val Ala Ala His Glu Phe  
 210 215 220  
 Gly His Ser Leu Gly Leu Asp His Ser Lys Asp Pro Gly Ala Leu Met  
 225 230 235 240  
 Phe Pro Ile Tyr Thr Tyr Thr Gly Lys Ser His Phe Met Leu Pro Asp  
 245 250 255  
 Asp Asp Val Gln Gly Ile Gln Ser Leu Tyr Gly Pro Gly Asp Glu Asp  
 260 265 270  
 Pro Asn Pro Lys His Pro Lys Thr Pro Asp Lys Cys Asp Pro Ser Leu  
 275 280 285  
 Ser Leu Asp Ala Ile Thr Ser Leu Arg Gly Glu Thr Met Ile Phe Lys  
 290 295 300  
 Asp Arg Phe Phe Trp Arg Leu His Pro Gln Gln Val Asp Ala Glu Leu  
 305 310 315 320  
 Phe Leu Thr Lys Ser Phe Trp Pro Glu Leu Pro Asn Arg Ile Asp Ala  
 325 330 335  
 Ala Tyr Glu His Pro Ser His Asp Leu Ile Phe Ile Phe Arg Gly Arg  
 340 345 350  
 Lys Phe Trp Ala Leu Asn Gly Tyr Asp Ile Leu Glu Gly Tyr Pro Lys  
 355 360 365  
 Lys Ile Ser Glu Leu Gly Leu Pro Lys Glu Val Lys Lys Ile Ser Ala  
 370 375 380  
 Ala Val His Phe Glu Asp Thr Gly Lys Thr Leu Leu Phe Ser Gly Asn  
 385 390 395 400  
 Gln Val Trp Arg Tyr Asp Asp Thr Asn His Ile Met Asp Lys Asp Tyr  
 405 410 415  
 Pro Arg Leu Ile Glu Glu Asp Phe Pro Gly Ile Gly Asp Lys Val Asp  
 420 425 430  
 Ala Val Tyr Glu Lys Asn Gly Tyr Ile Tyr Phe Phe Asn Gly Pro Ile  
 435 440 445  
 Gln Phe Glu Tyr Ser Ile Trp Ser Asn Arg Ile Val Arg Val Met Pro  
 450 455 460  
 Ala Asn Ser Ile Leu Trp Cys  
 465 470

&lt;210&gt; 326

&lt;211&gt; 418

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<400> 326  
 Met Arg Ser Leu Leu Leu Leu Ser Ala Phe Cys Leu Leu Glu Ala Ala  
 1 5 10 15  
 Leu Ala Ala Glu Val Lys Lys Pro Ala Ala Ala Ala Pro Gly Thr  
 20 25 30  
 Ala Glu Lys Leu Ser Pro Lys Ala Ala Thr Leu Ala Glu Arg Ser Ala  
 35 40 45  
 Gly Leu Ala Phe Ser Leu Tyr Gln Ala Met Ala Lys Asp Gln Ala Val  
 50 55 60  
 Glu Asn Ile Leu Val Ser Pro Val Val Val Ala Ser Ser Leu Gly Leu  
 65 70 75 80  
 Val Ser Leu Gly Gly Lys Ala Thr Thr Ala Ser Gln Ala Lys Ala Val  
 85 90 95  
 Leu Ser Ala Glu Gln Leu Arg Asp Glu Glu Val His Ala Gly Leu Gly  
 100 105 110  
 Glu Leu Leu Arg Ser Leu Ser Asn Ser Thr Ala Arg Asn Val Thr Trp  
 115 120 125  
 Lys Leu Gly Ser Arg Leu Tyr Gly Pro Ser Ser Val Ser Phe Ala Asp  
 130 135 140  
 Asp Phe Val Arg Ser Ser Lys Gln His Tyr Asn Cys Glu His Ser Lys  
 145 150 155 160  
 Ile Asn Phe Arg Asp Lys Arg Ser Ala Leu Gln Ser Ile Asn Glu Trp  
 165 170 175  
 Ala Ala Gln Thr Thr Asp Gly Lys Leu Pro Glu Val Thr Lys Asp Val  
 180 185 190  
 Glu Arg Thr Asp Gly Ala Leu Leu Val Asn Ala Met Phe Lys Pro  
 195 200 205  
 His Trp Asp Glu Lys Phe His His Lys Met Val Asp Asn Arg Gly Phe  
 210 215 220  
 Met Val Thr Arg Ser Tyr Thr Val Gly Val Met Met Met His Arg Thr  
 225 230 235 240  
 Gly Leu Tyr Asn Tyr Tyr Asp Asp Glu Lys Glu Lys Leu Gln Ile Val  
 245 250 255  
 Glu Met Pro Leu Ala His Lys Leu Ser Ser Leu Ile Ile Leu Met Pro  
 260 265 270  
 His His Val Glu Pro Leu Glu Arg Leu Glu Lys Leu Leu Thr Lys Glu  
 275 280 285  
 Gln Leu Lys Ile Trp Met Gly Lys Met Gln Lys Lys Ala Val Ala Ile  
 290 295 300  
 Ser Leu Pro Lys Gly Val Val Glu Val Thr His Asp Leu Gln Lys His  
 305 310 315 320  
 Leu Ala Gly Leu Gly Leu Thr Glu Ala Ile Asp Lys Asn Lys Ala Asp  
 325 330 335  
 Leu Ser Arg Met Ser Gly Lys Lys Asp Leu Tyr Leu Ala Ser Val Phe  
 340 345 350  
 His Ala Thr Ala Phe Glu Leu Asp Thr Asp Gly Asn Pro Phe Asp Gln  
 355 360 365  
 Asp Ile Tyr Gly Arg Glu Glu Leu Arg Ser Pro Lys Leu Phe Tyr Ala  
 370 375 380  
 Asp His Pro Phe Ile Phe Leu Val Arg Asp Thr Gln Ser Gly Ser Leu  
 385 390 395 400  
 Leu Phe Ile Gly Arg Leu Val Arg Pro Lys Gly Asp Lys Met Arg Asp  
 405 410 415  
 Glu Leu

&lt;210&gt; 327

&lt;211&gt; 314

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 327

Met Asp Ala Phe Lys Gly Gly Met Ser Leu Glu Arg Leu Pro Glu Gly  
 1 5 10 15  
 Leu Arg Pro Pro Pro Pro Pro His Asp Met Gly Pro Ala Phe His  
 20 25 30  
 Leu Ala Arg Pro Ala Asp Pro Arg Glu Pro Leu Glu Asn Ser Ala Ser  
 35 40 45  
 Glu Ser Ser Asp Thr Glu Leu Pro Glu Lys Glu Arg Gly Gly Glu Pro  
 50 55 60  
 Lys Gly Pro Glu Asp Ser Gly Ala Gly Gly Thr Gly Cys Gly Gly Ala  
 65 70 75 80  
 Asp Asp Pro Ala Lys Lys Lys Lys Gln Arg Arg Gln Arg Thr His Phe  
 85 90 95  
 Thr Ser Gln Gln Leu Gln Glu Leu Glu Ala Thr Phe Gln Arg Asn Arg  
 100 105 110  
 Tyr Pro Asp Met Ser Met Arg Glu Glu Ile Ala Val Trp Thr Asn Leu  
 115 120 125  
 Thr Glu Pro Arg Val Arg Val Trp Phe Lys Asn Arg Arg Ala Lys Trp  
 130 135 140  
 Arg Lys Arg Glu Arg Asn Gln Gln Leu Asp Leu Cys Lys Gly Gly Tyr  
 145 150 155 160  
 Val Pro Gln Phe Ser Gly Leu Val Gln Pro Tyr Glu Asp Val Tyr Ala  
 165 170 175  
 Ala Gly Tyr Ser Tyr Asn Asn Trp Ala Ala Lys Ser Leu Ala Pro Ala  
 180 185 190  
 Pro Leu Ser Thr Lys Ser Phe Thr Phe Phe Asn Ser Met Ser Pro Leu  
 195 200 205  
 Ser Ser Gln Ser Met Phe Ser Ala Pro Ser Ser Ile Ser Ser Met Thr  
 210 215 220  
 Met Pro Ser Ser Met Gly Pro Gly Ala Val Pro Gly Met Pro Asn Ser  
 225 230 235 240  
 Gly Leu Asn Asn Ile Asn Asn Leu Thr Gly Ser Ser Leu Asn Ser Ala  
 245 250 255  
 Met Ser Pro Gly Ala Cys Pro Tyr Gly Thr Pro Ala Ser Pro Tyr Ser  
 260 265 270  
 Val Tyr Arg Asp Thr Cys Asn Ser Ser Leu Ala Ser Leu Arg Leu Lys  
 275 280 285  
 Ser Lys Gln His Ser Ser Phe Gly Tyr Gly Ala Leu Gln Gly Pro Ala  
 290 295 300  
 Ser Gly Leu Asn Ala Cys Gln Tyr Asn Ser  
 305 310

&lt;210&gt; 328

&lt;211&gt; 2828

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 328

Met	Pro	Lys	Arg	Ala	His	Trp	Gly	Ala	Leu	Ser	Val	Val	Leu	Ile	Leu
1				5					10					15	
Leu	Trp	Gly	His	Pro	Arg	Val	Ala	Leu	Ala	Cys	Pro	His	Pro	Cys	Ala
			20					25					30		
Cys	Tyr	Val	Pro	Ser	Glu	Val	His	Cys	Thr	Phe	Arg	Ser	Leu	Ala	Ser
		35					40					45			
Val	Pro	Ala	Gly	Ile	Ala	Arg	His	Val	Glu	Arg	Ile	Asn	Leu	Gly	Phe
		50				55					60				
Asn	Ser	Ile	Gln	Ala	Leu	Ser	Glu	Thr	Ser	Phe	Ala	Gly	Leu	Thr	Lys
65					70					75					80
Leu	Glu	Leu	Leu	Met	Ile	His	Gly	Asn	Glu	Ile	Pro	Ser	Ile	Pro	Asp
				85				90						95	
Gly	Ala	Leu	Arg	Asp	Leu	Ser	Ser	Leu	Gln	Val	Phe	Lys	Phe	Ser	Tyr
			100					105					110		
Asn	Lys	Leu	Arg	Val	Ile	Thr	Gly	Gln	Thr	Leu	Gln	Gly	Leu	Ser	Asn
		115					120					125			
Leu	Met	Arg	Leu	His	Ile	Asp	His	Asn	Lys	Ile	Glu	Phe	Ile	His	Pro
		130				135					140				
Gln	Ala	Phe	Asn	Gly	Leu	Thr	Ser	Leu	Arg	Leu	Leu	His	Leu	Glu	Gly
145					150					155					160
Asn	Leu	Leu	His	Gln	Leu	His	Pro	Ser	Thr	Phe	Ser	Thr	Phe	Thr	Phe
				165				170						175	
Leu	Asp	Tyr	Phe	Arg	Leu	Ser	Thr	Ile	Arg	His	Leu	Tyr	Leu	Ala	Glu
			180					185					190		
Asn	Met	Val	Arg	Thr	Leu	Pro	Ala	Ser	Met	Leu	Arg	Asn	Met	Pro	Leu
		195					200					205			
Leu	Glu	Asn	Leu	Tyr	Leu	Gln	Gly	Asn	Pro	Trp	Thr	Cys	Asp	Cys	Glu
		210				215					220				
Met	Arg	Trp	Phe	Leu	Glu	Trp	Asp	Ala	Lys	Ser	Arg	Gly	Ile	Leu	Lys
225					230					235					240
Cys	Lys	Lys	Asp	Lys	Ala	Tyr	Glu	Gly	Gly	Gln	Leu	Cys	Ala	Met	Cys
				245				250						255	
Phe	Ser	Pro	Lys	Lys	Leu	Tyr	Lys	His	Glu	Ile	His	Lys	Leu	Lys	Asp
			260					265					270		
Met	Thr	Cys	Leu	Lys	Pro	Ser	Ile	Glu	Ser	Pro	Leu	Arg	Gln	Asn	Arg
		275					280					285			
Ser	Arg	Ser	Ile	Glu	Glu	Glu	Gln	Glu	Gln	Glu	Glu	Asp	Gly	Gly	Ser
		290				295					300				
Gln	Leu	Ile	Leu	Glu	Lys	Phe	Gln	Leu	Pro	Gln	Trp	Ser	Ile	Ser	Leu
305					310					315					320
Asn	Met	Thr	Asp	Glu	His	Gly	Asn	Met	Val	Asn	Leu	Val	Cys	Asp	Ile
				325				330						335	
Lys	Lys	Pro	Met	Asp	Val	Tyr	Lys	Ile	His	Leu	Asn	Gln	Thr	Asp	Pro
			340					345					350		
Pro	Asp	Ile	Asp	Ile	Asn	Ala	Thr	Val	Ala	Leu	Asp	Phe	Glu	Cys	Pro
		355					360					365			
Met	Thr	Arg	Glu	Asn	Tyr	Glu	Lys	Leu	Trp	Lys	Leu	Ile	Ala	Tyr	Tyr
		370				375					380				
Ser	Glu	Val	Pro	Val	Lys	Leu	His	Arg	Glu	Leu	Met	Leu	Ser	Lys	Asp
385					390					395					400
Pro	Arg	Val	Ser	Tyr	Gln	Tyr	Arg	Gln	Asp	Ala	Asp	Glu	Glu	Ala	Leu
				405				410						415	
Tyr	Tyr	Thr	Gly	Val	Arg	Ala	Gln	Ile	Leu	Ala	Glu	Pro	Glu	Trp	Val
			420					425					430		
Met	Gln	Pro	Ser	Ile	Asp	Ile	Gln	Leu	Asn	Arg	Arg	Gln	Ser	Thr	Ala
		435					440					445			
Lys	Lys	Val	Leu	Leu	Ser	Tyr	Tyr	Thr	Gln	Tyr	Ser	Gln	Thr	Ile	Ser
		450				455					460				
Thr	Lys	Asp	Thr	Arg	Gln	Ala	Arg	Gly	Arg	Ser	Trp	Val	Met	Ile	Glu
465					470					475					480

Pro Ser Gly Ala Val Gln Arg Asp Gln Thr Val Leu Glu Gly Gly Pro  
 485 490 495  
 Cys Gln Leu Ser Cys Asn Val Lys Ala Ser Glu Ser Pro Ser Ile Phe  
 500 505 510  
 Trp Val Leu Pro Asp Gly Ser Ile Leu Lys Ala Pro Met Asp Asp Pro  
 515 520 525  
 Asp Ser Lys Phe Ser Ile Leu Ser Ser Gly Trp Leu Arg Ile Lys Ser  
 530 535 540  
 Met Glu Pro Ser Asp Ser Gly Leu Tyr Gln Cys Ile Ala Gln Val Arg  
 545 550 555 560  
 Asp Glu Met Asp Arg Met Val Tyr Arg Val Leu Val Gln Ser Pro Ser  
 565 570 575  
 Thr Gln Pro Ala Glu Lys Asp Thr Val Thr Ile Gly Lys Asn Pro Gly  
 580 585 590  
 Glu Ser Val Thr Leu Pro Cys Asn Ala Leu Ala Ile Pro Glu Ala His  
 595 600 605  
 Leu Ser Trp Ile Leu Pro Asn Arg Arg Ile Ile Asn Asp Leu Ala Asn  
 610 615 620  
 Thr Ser His Val Tyr Met Leu Pro Asn Gly Thr Leu Ser Ile Pro Lys  
 625 630 635 640  
 Val Gln Val Ser Asp Ser Gly Tyr Tyr Arg Cys Val Ala Val Asn Gln  
 645 650 655  
 Gln Gly Ala Asp His Phe Thr Val Gly Ile Thr Val Thr Lys Lys Gly  
 660 665 670  
 Ser Gly Leu Pro Ser Lys Arg Gly Arg Arg Pro Gly Ala Lys Ala Leu  
 675 680 685  
 Ser Arg Val Arg Glu Asp Ile Val Glu Asp Glu Gly Ser Gly Met  
 690 695 700  
 Gly Asp Glu Glu Asn Thr Ser Arg Arg Leu Leu His Pro Lys Asp Gln  
 705 710 715 720  
 Glu Val Phe Leu Lys Thr Lys Asp Asp Ala Ile Asn Gly Asp Lys Lys  
 725 730 735  
 Ala Lys Lys Gly Arg Arg Lys Leu Lys Leu Trp Lys His Ser Glu Lys  
 740 745 750  
 Glu Pro Glu Thr Asn Val Ala Glu Gly Arg Arg Val Phe Glu Ser Arg  
 755 760 765  
 Arg Arg Ile Asn Met Ala Asn Lys Gln Ile Asn Pro Glu Arg Trp Ala  
 770 775 780  
 Asp Ile Leu Ala Lys Val Arg Gly Lys Asn Leu Pro Lys Gly Thr Glu  
 785 790 795 800  
 Val Pro Pro Leu Ile Lys Thr Thr Ser Pro Pro Ser Leu Ser Leu Glu  
 805 810 815  
 Val Thr Pro Pro Phe Pro Ala Val Ser Pro Pro Ser Ala Ser Pro Val  
 820 825 830  
 Gln Thr Val Thr Ser Ala Glu Glu Ser Ser Ala Asp Val Pro Leu Leu  
 835 840 845  
 Gly Glu Glu Glu His Val Leu Gly Thr Ile Ser Ser Ala Ser Met Gly  
 850 855 860  
 Leu Glu His Asn His Asn Gly Val Ile Leu Val Glu Pro Glu Val Thr  
 865 870 875 880  
 Ser Thr Pro Leu Glu Glu Val Val Asp Asp Leu Ser Glu Lys Thr Glu  
 885 890 895  
 Glu Ile Thr Ser Thr Glu Gly Asp Leu Lys Gly Thr Ala Ala Pro Thr  
 900 905 910  
 Leu Ile Ser Glu Pro Tyr Glu Pro Ser Pro Thr Leu His Thr Leu Asp  
 915 920 925  
 Thr Val Tyr Glu Lys Pro Thr His Glu Glu Thr Ala Thr Glu Gly Trp  
 930 935 940  
 Ser Ala Ala Asp Val Gly Ser Ser Pro Glu Pro Thr Ser Ser Glu Tyr  
 945 950 955 960  
 Glu Pro Pro Leu Asp Ala Val Ser Leu Ala Glu Ser Glu Pro Met Gln  
 965 970 975

Tyr	Phe	Asp	Pro	Asp	Leu	Glu	Thr	Lys	Ser	Gln	Pro	Asp	Glu	Asp	Lys
			980												
Met	Lys	Glu	Asp	Thr	Phe	Ala	His	Leu	Thr	Pro	Thr	Pro	Thr	Ile	Trp
			995												
Val	Asn	Asp	Ser	Ser	Thr	Ser	Gln	Leu	Phe	Glu	Asp	Ser	Thr	Ile	
	1010					1015					1020				
Gly	Glu	Pro	Gly	Val	Pro	Gly	Gln	Ser	His	Leu	Gln	Gly	Leu	Thr	
	1025					1030					1035				
Asp	Asn	Ile	His	Leu	Val	Lys	Ser	Ser	Leu	Ser	Thr	Gln	Asp	Thr	
	1040					1045					1050				
Leu	Leu	Ile	Lys	Lys	Gly	Met	Lys	Glu	Met	Ser	Gln	Thr	Leu	Gln	
	1055					1060					1065				
Gly	Gly	Asn	Met	Leu	Glu	Gly	Asp	Pro	Thr	His	Ser	Arg	Ser	Ser	
	1070					1075					1080				
Glu	Ser	Glu	Gly	Gln	Glu	Ser	Lys	Ser	Ile	Thr	Leu	Pro	Asp	Ser	
	1085					1090					1095				
Thr	Leu	Gly	Ile	Met	Ser	Ser	Met	Ser	Pro	Val	Lys	Lys	Pro	Ala	
	1100					1105					1110				
Glu	Thr	Thr	Val	Gly	Thr	Leu	Leu	Asp	Lys	Asp	Thr	Thr	Thr	Val	
	1115					1120					1125				
Thr	Thr	Thr	Pro	Arg	Gln	Lys	Val	Ala	Pro	Ser	Ser	Thr	Met	Ser	
	1130					1135					1140				
Thr	His	Pro	Ser	Arg	Arg	Arg	Pro	Asn	Gly	Arg	Arg	Arg	Leu	Arg	
	1145					1150					1155				
Pro	Asn	Lys	Phe	Arg	His	Arg	His	Lys	Gln	Thr	Pro	Pro	Thr	Thr	
	1160					1165					1170				
Phe	Ala	Pro	Ser	Glu	Thr	Phe	Ser	Thr	Gln	Pro	Thr	Gln	Ala	Pro	
	1175					1180					1185				
Asp	Ile	Lys	Ile	Ser	Ser	Gln	Val	Glu	Ser	Ser	Leu	Val	Pro	Thr	
	1190					1195					1200				
Ala	Trp	Val	Asp	Asn	Thr	Val	Asn	Thr	Pro	Lys	Gln	Leu	Glu	Met	
	1205					1210					1215				
Glu	Lys	Asn	Ala	Glu	Pro	Thr	Ser	Lys	Gly	Thr	Pro	Arg	Arg	Lys	
	1220					1225					1230				
His	Gly	Lys	Arg	Pro	Asn	Lys	His	Arg	Tyr	Thr	Pro	Ser	Thr	Val	
	1235					1240					1245				
Ser	Ser	Arg	Ala	Ser	Gly	Ser	Lys	Pro	Ser	Pro	Ser	Pro	Glu	Asn	
	1250					1255					1260				
Lys	His	Arg	Asn	Ile	Val	Thr	Pro	Ser	Ser	Glu	Thr	Ile	Leu	Leu	
	1265					1270					1275				
Pro	Arg	Thr	Val	Ser	Leu	Lys	Thr	Glu	Gly	Pro	Tyr	Asp	Ser	Leu	
	1280					1285					1290				
Asp	Tyr	Met	Thr	Thr	Thr	Arg	Lys	Ile	Tyr	Ser	Ser	Tyr	Pro	Lys	
	1295					1300					1305				
Val	Gln	Glu	Thr	Leu	Pro	Val	Thr	Tyr	Lys	Pro	Thr	Ser	Asp	Gly	
	1310					1315					1320				
Lys	Glu	Ile	Lys	Asp	Asp	Val	Ala	Thr	Asn	Val	Asp	Lys	His	Lys	
	1325					1330					1335				
Ser	Asp	Ile	Leu	Val	Thr	Gly	Glu	Ser	Ile	Thr	Asn	Ala	Ile	Pro	
	1340					1345					1350				
Thr	Ser	Arg	Ser	Leu	Val	Ser	Thr	Met	Gly	Glu	Phe	Lys	Glu	Glu	
	1355					1360					1365				
Ser	Ser	Pro	Val	Gly	Phe	Pro	Gly	Thr	Pro	Thr	Trp	Asn	Pro	Ser	
	1370					1375					1380				
Arg	Thr	Ala	Gln	Pro	Gly	Arg	Leu	Gln	Thr	Asp	Ile	Pro	Val	Thr	
	1385					1390					1395				
Thr	Ser	Gly	Glu	Asn	Leu	Thr	Asp	Pro	Pro	Leu	Leu	Lys	Glu	Leu	
	1400					1405					1410				
Glu	Asp	Val	Asp	Phe	Thr	Ser	Glu	Phe	Leu	Ser	Ser	Leu	Thr	Val	
	1415					1420					1425				
Ser	Thr	Pro	Phe	His	Gln	Glu	Glu	Ala	Gly	Ser	Ser	Thr	Thr	Leu	
	1430					1435					1440				



Ser	Ser	Ile	Lys	Val	Glu	Val	Ala	Ser	Ser	Gln	Ala	Glu	Thr	Thr
1445	1445					1450					1455			
Thr	Leu	Asp	Gln	Asp	His	Leu	Glu	Thr	Thr	Val	Ala	Ile	Leu	Leu
1460	1460					1465					1470			
Ser	Glu	Thr	Arg	Pro	Gln	Asn	His	Thr	Pro	Thr	Ala	Ala	Arg	Met
1475	1475					1480					1485			
Lys	Glu	Pro	Ala	Ser	Ser	Ser	Pro	Ser	Thr	Ile	Leu	Met	Ser	Leu
1490	1490					1495					1500			
Gly	Gln	Thr	Thr	Thr	Thr	Lys	Pro	Ala	Leu	Pro	Ser	Pro	Arg	Ile
1505	1505					1510					1515			
Ser	Gln	Ala	Ser	Arg	Asp	Ser	Lys	Glu	Asn	Val	Phe	Leu	Asn	Tyr
1520	1520					1525					1530			
Val	Gly	Asn	Pro	Glu	Thr	Glu	Ala	Thr	Pro	Val	Asn	Asn	Glu	Gly
1535	1535					1540					1545			
Thr	Gln	His	Met	Ser	Gly	Pro	Asn	Glu	Leu	Ser	Thr	Pro	Ser	Ser
1550	1550					1555					1560			
Asp	Arg	Asp	Ala	Phe	Asn	Leu	Ser	Thr	Lys	Leu	Glu	Leu	Glu	Lys
1565	1565					1570					1575			
Gln	Val	Phe	Gly	Ser	Arg	Ser	Leu	Pro	Arg	Gly	Pro	Asp	Ser	Gln
1580	1580					1585					1590			
Arg	Gln	Asp	Gly	Arg	Val	His	Ala	Ser	His	Gln	Leu	Thr	Arg	Val
1595	1595					1600					1605			
Pro	Ala	Lys	Pro	Ile	Leu	Pro	Thr	Ala	Thr	Val	Arg	Leu	Pro	Glu
1610	1610					1615					1620			
Met	Ser	Thr	Gln	Ser	Ala	Ser	Arg	Tyr	Phe	Val	Thr	Ser	Gln	Ser
1625	1625					1630					1635			
Pro	Arg	His	Trp	Thr	Asn	Lys	Pro	Glu	Ile	Thr	Thr	Tyr	Pro	Ser
1640	1640					1645					1650			
Gly	Ala	Leu	Pro	Glu	Asn	Lys	Gln	Phe	Thr	Thr	Pro	Arg	Leu	Ser
1655	1655					1660					1665			
Ser	Thr	Thr	Ile	Pro	Leu	Pro	Leu	His	Met	Ser	Lys	Pro	Ser	Ile
1670	1670					1675					1680			
Pro	Ser	Lys	Phe	Thr	Asp	Arg	Arg	Thr	Asp	Gln	Phe	Asn	Gly	Tyr
1685	1685					1690					1695			
Ser	Lys	Val	Phe	Gly	Asn	Asn	Asn	Ile	Pro	Glu	Ala	Arg	Asn	Pro
1700	1700					1705					1710			
Val	Gly	Lys	Pro	Pro	Ser	Pro	Arg	Ile	Pro	His	Tyr	Ser	Asn	Gly
1715	1715					1720					1725			
Arg	Leu	Pro	Phe	Phe	Thr	Asn	Lys	Thr	Leu	Ser	Phe	Pro	Gln	Leu
1730	1730					1735					1740			
Gly	Val	Thr	Arg	Arg	Pro	Gln	Ile	Pro	Thr	Ser	Pro	Ala	Pro	Val
1745	1745					1750					1755			
Met	Arg	Glu	Arg	Lys	Val	Ile	Pro	Gly	Ser	Tyr	Asn	Arg	Ile	His
1760	1760					1765					1770			
Ser	His	Ser	Thr	Phe	His	Leu	Asp	Phe	Gly	Pro	Pro	Ala	Pro	Pro
1775	1775					1780					1785			
Leu	Leu	His	Thr	Pro	Gln	Thr	Thr	Gly	Ser	Pro	Ser	Thr	Asn	Leu
1790	1790					1795					1800			
Gln	Asn	Ile	Pro	Met	Val	Ser	Ser	Thr	Gln	Ser	Ser	Ile	Ser	Phe
1805	1805					1810					1815			
Ile	Thr	Ser	Ser	Val	Gln	Ser	Ser	Gly	Ser	Phe	His	Gln	Ser	Ser
1820	1820					1825					1830			
Ser	Lys	Phe	Phe	Ala	Gly	Gly	Pro	Pro	Ala	Ser	Lys	Phe	Trp	Ser
1835	1835					1840					1845			
Leu	Gly	Glu	Lys	Pro	Gln	Ile	Leu	Thr	Lys	Ser	Pro	Gln	Thr	Val
1850	1850					1855					1860			
Ser	Val	Thr	Ala	Glu	Thr	Asp	Thr	Val	Phe	Pro	Cys	Glu	Ala	Thr
1865	1865					1870					1875			
Gly	Lys	Pro	Lys	Pro	Phe	Val	Thr	Trp	Thr	Lys	Val	Ser	Thr	Gly
1880	1880					1885					1890			
Ala	Leu	Met	Thr	Pro	Asn	Thr	Arg	Ile	Gln	Arg	Phe	Glu	Val	Leu
1895	1895					1900					1905			

Lys	Asn	Gly	Thr	Leu	Val	Ile	Arg	Lys	Val	Gln	Val	Gln	Asp	Arg
1910						1915					1920			
Gly	Gln	Tyr	Met	Cys	Thr	Ala	Ser	Asn	Leu	His	Gly	Leu	Asp	Arg
1925						1930					1935			
Met	Val	Val	Leu	Leu	Ser	Val	Thr	Val	Gln	Gln	Pro	Gln	Ile	Leu
1940						1945					1950			
Ala	Ser	His	Tyr	Gln	Asp	Val	Thr	Val	Tyr	Leu	Gly	Asp	Thr	Ile
1955						1960					1965			
Ala	Met	Glu	Cys	Leu	Ala	Lys	Gly	Thr	Pro	Ala	Pro	Gln	Ile	Ser
1970						1975					1980			
Trp	Ile	Phe	Pro	Asp	Arg	Arg	Val	Trp	Gln	Thr	Val	Ser	Pro	Val
1985						1990					1995			
Glu	Ser	Arg	Ile	Thr	Leu	His	Glu	Asn	Arg	Thr	Leu	Ser	Ile	Lys
2000						2005					2010			
Glu	Ala	Ser	Phe	Ser	Asp	Arg	Gly	Val	Tyr	Lys	Cys	Val	Ala	Ser
2015						2020					2025			
Asn	Ala	Ala	Gly	Ala	Asp	Ser	Leu	Ala	Ile	Arg	Leu	His	Val	Ala
2030						2035					2040			
Ala	Leu	Pro	Pro	Val	Ile	His	Gln	Glu	Lys	Leu	Glu	Asn	Ile	Ser
2045						2050					2055			
Leu	Pro	Pro	Gly	Leu	Ser	Ile	His	Ile	His	Cys	Thr	Ala	Lys	Ala
2060						2065					2070			
Ala	Pro	Leu	Pro	Ser	Val	Arg	Trp	Val	Leu	Gly	Asp	Gly	Thr	Gln
2075						2080					2085			
Ile	Arg	Pro	Ser	Gln	Phe	Leu	His	Gly	Asn	Leu	Phe	Val	Phe	Pro
2090						2095					2100			
Asn	Gly	Thr	Leu	Tyr	Ile	Arg	Asn	Leu	Ala	Pro	Lys	Asp	Ser	Gly
2105						2110					2115			
Arg	Tyr	Glu	Cys	Val	Ala	Ala	Asn	Leu	Val	Gly	Ser	Ala	Arg	Arg
2120						2125					2130			
Thr	Val	Gln	Leu	Asn	Val	Gln	Arg	Ala	Ala	Ala	Asn	Ala	Arg	Ile
2135						2140					2145			
Thr	Gly	Thr	Ser	Pro	Arg	Arg	Thr	Asp	Val	Arg	Tyr	Gly	Gly	Thr
2150						2155					2160			
Leu	Lys	Leu	Asp	Cys	Ser	Ala	Ser	Gly	Asp	Pro	Trp	Pro	Arg	Ile
2165						2170					2175			
Leu	Trp	Arg	Leu	Pro	Ser	Lys	Arg	Met	Ile	Asp	Ala	Leu	Phe	Ser
2180						2185					2190			
Phe	Asp	Ser	Arg	Ile	Lys	Val	Phe	Ala	Asn	Gly	Thr	Leu	Val	Val
2195						2200					2205			
Lys	Ser	Val	Thr	Asp	Lys	Asp	Ala	Gly	Asp	Tyr	Leu	Cys	Val	Ala
2210						2215					2220			
Arg	Asn	Lys	Val	Gly	Asp	Asp	Tyr	Val	Val	Leu	Lys	Val	Asp	Val
2225						2230					2235			
Val	Met	Lys	Pro	Ala	Lys	Ile	Glu	His	Lys	Glu	Glu	Asn	Asp	His
2240						2245					2250			
Lys	Val	Phe	Tyr	Gly	Gly	Asp	Leu	Lys	Val	Asp	Cys	Val	Ala	Thr
2255						2260					2265			
Gly	Leu	Pro	Asn	Pro	Glu	Ile	Ser	Trp	Ser	Leu	Pro	Asp	Gly	Ser
2270						2275					2280			
Leu	Val	Asn	Ser	Phe	Met	Gln	Ser	Asp	Asp	Ser	Gly	Gly	Arg	Thr
2285						2290					2295			
Lys	Arg	Tyr	Val	Val	Phe	Asn	Asn	Gly	Thr	Leu	Tyr	Phe	Asn	Glu
2300						2305					2310			
Val	Gly	Met	Arg	Glu	Glu	Gly	Asp	Tyr	Thr	Cys	Phe	Ala	Glu	Asn
2315						2320					2325			
Gln	Val	Gly	Lys	Asp	Glu	Met	Arg	Val	Arg	Val	Lys	Val	Val	Thr
2330						2335					2340			
Ala	Pro	Ala	Thr	Ile	Arg	Asn	Lys	Thr	Tyr	Leu	Ala	Val	Gln	Val
2345						2350					2355			
Pro	Tyr	Gly	Asp	Val	Val	Thr	Val	Ala	Cys	Glu	Ala	Lys	Gly	Glu
2360						2365					2370			

Pro Met	Pro Lys Val Thr	Trp	Leu Ser Pro Thr	Asn	Lys Val Ile
2375		2380		2385	
Pro Thr	Ser Ser Glu Lys	Tyr	Gln Ile Tyr Gln	Asp	Gly Thr Leu
2390		2395		2400	
Leu Ile	Gln Lys Ala Gln	Arg	Ser Asp Ser Gly	Asn	Tyr Thr Cys
2405		2410		2415	
Leu Val	Arg Asn Ser Ala	Gly	Glu Asp Arg Lys	Thr	Val Trp Ile
2420		2425		2430	
His Val	Asn Val Gln Pro	Pro	Lys Ile Asn Gly	Asn	Pro Asn Pro
2435		2440		2445	
Ile Thr	Thr Val Arg Glu	Ile	Ala Ala Gly Gly	Ser	Arg Lys Leu
2450		2455		2460	
Ile Asp	Cys Lys Ala Glu	Gly	Ile Pro Thr Pro	Arg	Val Leu Trp
2465		2470		2475	
Ala Phe	Pro Glu Gly Val	Val	Leu Pro Ala Pro	Tyr	Tyr Gly Asn
2480		2485		2490	
Arg Ile	Thr Val His Gly	Asn	Gly Ser Leu Asp	Ile	Arg Ser Leu
2495		2500		2505	
Arg Lys	Ser Asp Ser Val	Gln	Leu Val Cys Met	Ala	Arg Asn Glu
2510		2515		2520	
Gly Gly	Glu Ala Arg Leu	Ile	Val Gln Leu Thr	Val	Leu Glu Pro
2525		2530		2535	
Met Glu	Lys Pro Ile Phe	His	Asp Pro Ile Ser	Glu	Lys Ile Thr
2540		2545		2550	
Ala Met	Ala Gly His Thr	Ile	Ser Leu Asn Cys	Ser	Ala Ala Gly
2555		2560		2565	
Thr Pro	Thr Pro Ser Leu	Val	Trp Val Leu Pro	Asn	Gly Thr Asp
2570		2575		2580	
Leu Gln	Ser Gly Gln Gln	Leu	Gln Arg Phe Tyr	His	Lys Ala Asp
2585		2590		2595	
Gly Met	Leu His Ile Ser	Gly	Leu Ser Ser Val	Asp	Ala Gly Ala
2600		2605		2610	
Tyr Arg	Cys Val Ala Arg	Asn	Ala Ala Gly His	Thr	Glu Arg Leu
2615		2620		2625	
Val Ser	Leu Lys Val Gly	Leu	Lys Pro Glu Ala	Asn	Lys Gln Tyr
2630		2635		2640	
His Asn	Leu Val Ser Ile	Ile	Asn Gly Glu Thr	Leu	Lys Leu Pro
2645		2650		2655	
Cys Thr	Pro Pro Gly Ala	Gly	Gln Gly Arg Phe	Ser	Trp Thr Leu
2660		2665		2670	
Pro Asn	Gly Met His Leu	Glu	Gly Pro Gln Thr	Leu	Gly Arg Val
2675		2680		2685	
Ser Leu	Leu Asp Asn Gly	Thr	Leu Thr Val Arg	Glu	Ala Ser Val
2690		2695		2700	
Phe Asp	Arg Gly Thr Tyr	Val	Cys Arg Met Glu	Thr	Glu Tyr Gly
2705		2710		2715	
Pro Ser	Val Thr Ser Ile	Pro	Val Ile Val Ile	Ala	Tyr Pro Pro
2720		2725		2730	
Arg Ile	Thr Ser Glu Pro	Thr	Pro Val Ile Tyr	Thr	Arg Pro Gly
2735		2740		2745	
Asn Thr	Val Lys Leu Asn	Cys	Met Ala Met Gly	Ile	Pro Lys Ala
2750		2755		2760	
Asp Ile	Thr Trp Glu Leu	Pro	Asp Lys Ser His	Leu	Lys Ala Gly
2765		2770		2775	
Val Gln	Ala Arg Leu Tyr	Gly	Asn Arg Phe Leu	His	Pro Gln Gly
2780		2785		2790	
Ser Leu	Thr Ile Gln His	Ala	Thr Gln Arg Asp	Ala	Gly Phe Tyr
2795		2800		2805	
Lys Cys	Met Ala Lys Asn	Ile	Leu Gly Ser Asp	Ser	Lys Thr Thr
2810		2815		2820	
Tyr Ile	His Val Phe				
2825					

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&lt;210&gt; 329

&lt;211&gt; 426

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 329

Met	Pro	Leu	Leu	Trp	Leu	Arg	Gly	Phe	Leu	Leu	Ala	Ser	Cys	Trp	Ile
1			5					10						15	
Ile	Val	Arg	Ser	Pro	Thr	Pro	Gly	Ser	Glu	Gly	His	Ser	Ala	Ala	
			20				25					30			
Pro	Asp	Cys	Pro	Ser	Cys	Ala	Leu	Ala	Ala	Leu	Pro	Lys	Asp	Val	Pro
		35				40					45				
Asn	Ser	Gln	Pro	Glu	Met	Val	Glu	Ala	Val	Lys	Lys	His	Ile	Leu	Asn
		50			55					60					
Met	Leu	His	Leu	Lys	Lys	Arg	Pro	Asp	Val	Thr	Gln	Pro	Val	Pro	Lys
65				70					75						80
Ala	Ala	Leu	Leu	Asn	Ala	Ile	Arg	Lys	Leu	His	Val	Gly	Lys	Val	Gly
			85					90					95		
Glu	Asn	Gly	Tyr	Val	Glu	Ile	Glu	Asp	Asp	Ile	Gly	Arg	Arg	Ala	Glu
			100				105					110			
Met	Asn	Glu	Leu	Met	Glu	Gln	Thr	Ser	Glu	Ile	Ile	Thr	Phe	Ala	Glu
		115				120						125			
Ser	Gly	Thr	Ala	Arg	Lys	Thr	Leu	His	Phe	Glu	Ile	Ser	Lys	Glu	Gly
		130			135						140				
Ser	Asp	Leu	Ser	Val	Val	Glu	Arg	Ala	Glu	Val	Trp	Leu	Phe	Leu	Lys
145				150						155					160
Val	Pro	Lys	Ala	Asn	Arg	Thr	Arg	Thr	Lys	Val	Thr	Ile	Arg	Leu	Phe
			165					170						175	
Gln	Gln	Gln	Lys	His	Pro	Gln	Gly	Ser	Leu	Asp	Thr	Gly	Glu	Glu	Ala
			180				185						190		
Glu	Glu	Val	Gly	Leu	Lys	Gly	Glu	Arg	Ser	Glu	Leu	Leu	Leu	Ser	Glu
		195				200					205				
Lys	Val	Val	Asp	Ala	Arg	Lys	Ser	Thr	Trp	His	Val	Phe	Pro	Val	Ser
		210			215						220				
Ser	Ser	Ile	Gln	Arg	Leu	Leu	Asp	Gln	Gly	Lys	Ser	Ser	Leu	Asp	Val
225				230					235					240	
Arg	Ile	Ala	Cys	Glu	Gln	Cys	Gln	Glu	Ser	Gly	Ala	Ser	Leu	Val	Leu
			245					250						255	
Leu	Gly	Lys	Lys	Lys	Lys	Lys	Glu	Glu	Gly	Glu	Gly	Lys	Lys	Lys	
		260					265					270			
Gly	Gly	Gly	Glu	Gly	Gly	Ala	Gly	Ala	Asp	Glu	Glu	Lys	Glu	Gln	Ser
		275				280						285			
His	Arg	Pro	Phe	Leu	Met	Leu	Gln	Ala	Arg	Gln	Ser	Glu	Asp	His	Pro
		290			295						300				
His	Arg	Arg	Arg	Arg	Arg	Gly	Leu	Glu	Cys	Asp	Gly	Lys	Val	Asn	Ile
305				310					315					320	
Cys	Cys	Lys	Lys	Gln	Phe	Phe	Val	Ser	Phe	Lys	Asp	Ile	Gly	Trp	Asn
			325					330						335	
Asp	Trp	Ile	Ile	Ala	Pro	Ser	Gly	Tyr	His	Ala	Asn	Tyr	Cys	Glu	Gly
		340					345					350			
Glu	Cys	Pro	Ser	His	Ile	Ala	Gly	Thr	Ser	Gly	Ser	Ser	Leu	Ser	Phe
		355				360					365				
His	Ser	Thr	Val	Ile	Asn	His	Tyr	Arg	Met	Arg	Gly	His	Ser	Pro	Phe
	370				375						380				
Ala	Asn	Leu	Lys	Ser	Cys	Cys	Val	Pro	Thr	Lys	Leu	Arg	Pro	Met	Ser
385				390						395					400

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Met Leu Tyr Tyr Asp Asp Gly Gln Asn Ile Ile Lys Lys Asp Ile Gln  
 405 410 415  
 Asn Met Ile Val Glu Glu Cys Gly Cys Ser  
 420 425

&lt;210&gt; 330

&lt;211&gt; 6792

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 330

Met Phe Ile Asn Ile Lys Ser Ile Leu Trp Met Cys Ser Thr Leu Ile  
 1 5 10 15  
 Val Thr His Ala Leu His Lys Val Lys Val Gly Lys Ser Pro Pro Val  
 20 25 30  
 Arg Gly Ser Leu Ser Gly Lys Val Ser Leu Pro Cys His Phe Ser Thr  
 35 40 45  
 Met Pro Thr Leu Pro Pro Ser Tyr Asn Thr Ser Glu Phe Leu Arg Ile  
 50 55 60  
 Lys Trp Ser Lys Ile Glu Val Asp Lys Asn Gly Lys Asp Leu Lys Glu  
 65 70 75 80  
 Thr Thr Val Leu Val Ala Gln Asn Gly Asn Ile Lys Ile Gly Gln Asp  
 85 90 95  
 Tyr Lys Gly Arg Val Ser Val Pro Thr His Pro Glu Ala Val Gly Asp  
 100 105 110  
 Ala Ser Leu Thr Val Val Lys Leu Leu Ala Ser Asp Ala Gly Leu Tyr  
 115 120 125  
 Arg Cys Asp Val Met Tyr Gly Ile Glu Asp Thr Gln Asp Thr Val Ser  
 130 135 140  
 Leu Thr Val Asp Gly Val Val Phe His Tyr Arg Ala Ala Thr Ser Arg  
 145 150 155 160  
 Tyr Thr Leu Asn Phe Glu Ala Ala Gln Lys Ala Cys Leu Asp Val Gly  
 165 170 175  
 Ala Val Ile Ala Thr Pro Glu Gln Leu Phe Ala Ala Tyr Glu Asp Gly  
 180 185 190  
 Phe Glu Gln Cys Asp Ala Gly Trp Leu Ala Asp Gln Thr Val Arg Tyr  
 195 200 205  
 Pro Ile Arg Ala Pro Arg Val Gly Cys Tyr Gly Asp Lys Met Gly Lys  
 210 215 220  
 Ala Gly Val Arg Thr Tyr Gly Phe Arg Ser Pro Gln Glu Thr Tyr Asp  
 225 230 235 240  
 Val Tyr Cys Tyr Val Asp His Leu Asp Gly Asp Val Phe His Leu Thr  
 245 250 255  
 Val Pro Ser Lys Phe Thr Phe Glu Glu Ala Ala Lys Glu Cys Glu Asn  
 260 265 270  
 Gln Asp Ala Arg Leu Ala Thr Val Gly Glu Leu Gln Ala Ala Trp Arg  
 275 280 285  
 Asn Gly Phe Asp Gln Cys Asp Tyr Gly Trp Leu Ser Asp Ala Ser Val  
 290 295 300  
 Arg His Pro Val Thr Val Ala Arg Ala Gln Cys Gly Gly Leu Leu  
 305 310 320  
 Gly Val Arg Thr Leu Tyr Arg Phe Glu Asn Gln Thr Gly Phe Pro Pro  
 325 330 335  
 Pro Asp Ser Arg Phe Asp Ala Tyr Cys Phe Lys Pro Lys Glu Ala Thr  
 340 345 350  
 Thr Ile Asp Leu Ser Ile Leu Ala Glu Thr Ala Ser Pro Ser Leu Ser  
 355 360 365

Lys	Glu	Pro	Gln	Met	Val	Ser	Asp	Arg	Thr	Thr	Pro	Ile	Ile	Pro	Leu
370						375					380				
Val	Asp	Glu	Leu	Pro	Val	Ile	Pro	Thr	Glu	Phe	Pro	Pro	Val	Gly	Asn
385					390					395					400
Ile	Val	Ser	Phe	Glu	Gln	Lys	Ala	Thr	Val	Gln	Pro	Gln	Ala	Ile	Thr
				405					410					415	
Asp	Ser	Leu	Ala	Thr	Lys	Leu	Pro	Thr	Pro	Thr	Gly	Ser	Thr	Lys	Lys
			420					425					430		
Pro	Trp	Asp	Met	Asp	Asp	Tyr	Ser	Pro	Ser	Ala	Ser	Gly	Pro	Leu	Gly
		435				440						445			
Lys	Leu	Asp	Ile	Ser	Glu	Ile	Lys	Glu	Glu	Val	Leu	Gln	Ser	Thr	Thr
		450				455					460				
Gly	Val	Ser	His	Tyr	Ala	Thr	Asp	Ser	Trp	Asp	Gly	Val	Val	Glu	Asp
465					470					475					480
Lys	Gln	Thr	Gln	Glu	Ser	Val	Thr	Gln	Ile	Glu	Gln	Ile	Glu	Val	Gly
				485					490					495	
Pro	Leu	Val	Thr	Ser	Met	Glu	Ile	Leu	Lys	His	Ile	Pro	Ser	Lys	Glu
			500					505					510		
Phe	Pro	Val	Thr	Glu	Thr	Pro	Leu	Val	Thr	Ala	Arg	Met	Ile	Leu	Glu
		515					520					525			
Ser	Lys	Thr	Glu	Lys	Lys	Met	Val	Ser	Thr	Val	Ser	Glu	Leu	Val	Thr
		530				535					540				
Thr	Gly	His	Tyr	Gly	Phe	Thr	Leu	Gly	Glu	Glu	Asp	Asp	Glu	Asp	Arg
545					550					555					560
Thr	Leu	Thr	Val	Gly	Ser	Asp	Glu	Ser	Thr	Leu	Ile	Phe	Asp	Gln	Ile
				565					570					575	
Pro	Glu	Val	Ile	Thr	Val	Ser	Lys	Thr	Ser	Glu	Asp	Thr	Ile	His	Thr
			580					585					590		
His	Leu	Glu	Asp	Leu	Glu	Ser	Val	Ser	Ala	Ser	Thr	Thr	Val	Ser	Pro
		595					600					605			
Leu	Ile	Met	Pro	Asp	Asn	Asn	Gly	Ser	Ser	Met	Asp	Asp	Trp	Glu	Glu
		610				615					620				
Arg	Gln	Thr	Ser	Gly	Arg	Ile	Thr	Glu	Glu	Phe	Leu	Gly	Lys	Tyr	Leu
625					630					635					640
Ser	Thr	Thr	Pro	Phe	Pro	Ser	Gln	His	Arg	Thr	Glu	Ile	Glu	Leu	Phe
				645					650					655	
Pro	Tyr	Ser	Gly	Asp	Lys	Ile	Leu	Val	Glu	Gly	Ile	Ser	Thr	Val	Ile
			660					665					670		
Tyr	Pro	Ser	Leu	Gln	Thr	Glu	Met	Thr	His	Arg	Arg	Glu	Arg	Thr	Glu
		675				680						685			
Thr	Leu	Ile	Pro	Glu	Met	Arg	Thr	Asp	Thr	Tyr	Thr	Asp	Glu	Ile	Gln
		690				695					700				
Glu	Glu	Ile	Thr	Lys	Ser	Pro	Phe	Met	Gly	Lys	Thr	Glu	Glu	Glu	Val
705					710					715					720
Phe	Ser	Gly	Met	Lys	Leu	Ser	Thr	Ser							

Leu	Glu	Glu	Val	Thr	Asp	Glu	Asp	Ile	Ala	Ala	His	Gly	Lys	Phe	Thr
865					870					875					880
Ile	Arg	Phe	Gln	Pro	Thr	Thr	Ser	Thr	Gly	Ile	Ala	Glu	Lys	Ser	Thr
			885						890						895
Leu	Arg	Asp	Ser	Thr	Thr	Glu	Glu	Lys	Val	Pro	Pro	Ile	Thr	Ser	Thr
			900					905							910
Glu	Gly	Gln	Val	Tyr	Ala	Thr	Met	Glu	Gly	Ser	Ala	Leu	Gly	Glu	Val
		915					920					925			
Glu	Asp	Val	Asp	Leu	Ser	Lys	Pro	Val	Ser	Thr	Val	Pro	Gln	Phe	Ala
	930					935					940				
His	Thr	Ser	Glu	Val	Glu	Gly	Leu	Ala	Phe	Val	Ser	Tyr	Ser	Ser	Thr
945					950					955					960
Gln	Glu	Pro	Thr	Thr	Tyr	Val	Asp	Ser	Ser	His	Thr	Ile	Pro	Leu	Ser
			965						970						975
Val	Ile	Pro	Lys	Thr	Asp	Trp	Gly	Val	Leu	Val	Pro	Ser	Val	Pro	Ser
			980					985							990
Glu	Asp	Glu	Val	Leu	Gly	Glu	Pro	Ser	Gln	Asp	Ile	Leu	Val	Ile	Asp
		995					1000								1005
Gln	Thr	Arg	Leu	Glu	Ala	Thr	Ile	Ser	Pro	Glu	Thr	Met	Arg	Thr	
	1010					1015						1020			
Thr	Lys	Ile	Thr	Glu	Gly	Thr	Thr	Gln	Glu	Glu	Phe	Pro	Trp	Lys	
	1025					1030						1035			
Glu	Gln	Thr	Ala	Glu	Lys	Pro	Val	Pro	Ala	Leu	Ser	Ser	Thr	Ala	
	1040					1045						1050			
Trp	Thr	Pro	Lys	Glu	Ala	Val	Thr	Pro	Leu	Asp	Glu	Gln	Glu	Gly	
	1055					1060						1065			
Asp	Gly	Ser	Ala	Tyr	Thr	Val	Ser	Glu	Asp	Glu	Leu	Leu	Thr	Gly	
	1070					1075						1080			
Ser	Glu	Arg	Val	Pro	Val	Leu	Glu	Thr	Thr	Pro	Val	Gly	Lys	Ile	
	1085					1090						1095			
Asp	His	Ser	Val	Ser	Tyr	Pro	Pro	Gly	Ala	Val	Thr	Glu	His	Lys	
	1100					1105						1110			
Val	Lys	Thr	Asp	Glu	Val	Val	Thr	Leu	Thr	Pro	Arg	Ile	Gly	Pro	
	1115					1120						1125			
Lys	Val	Ser	Leu	Ser	Pro	Gly	Pro	Glu	Gln	Lys	Tyr	Glu	Thr	Glu	
	1130					1135						1140			
Gly	Ser	Ser	Thr	Thr	Gly	Phe	Thr	Ser	Ser	Leu	Ser	Pro	Phe	Ser	
	1145					1150						1155			
Thr	His	Ile	Thr	Gln	Leu	Met	Glu	Glu	Thr	Thr	Thr	Glu	Lys	Thr	
	1160					1165						1170			
Ser	Leu	Glu	Asp	Ile	Asp	Leu	Gly	Ser	Gly	Leu	Phe	Glu	Lys	Pro	
	1175					1180						1185			
Lys	Ala	Thr	Glu	Leu	Ile	Glu	Phe	Ser	Thr	Ile	Lys	Val	Thr	Val	
	1190					1195						1200			
Pro	Ser	Asp	Ile	Thr	Thr	Ala	Phe	Ser	Ser	Val	Asp	Arg	Leu	His	
	1205					1210						1215			
Thr	Thr	Ser	Ala	Phe	Lys	Pro	Ser	Ser	Ala	Ile	Thr	Lys	Lys	Pro	
	1220					1225						1230			
Pro	Leu	Ile	Asp	Arg	Glu	Pro	Gly	Glu	Glu	Thr	Thr	Ser	Asp	Met	
	1235					1240						1245			
Val	Ile	Ile	Gly	Glu	Ser	Thr	Ser	His	Val	Pro	Pro	Thr	Thr	Leu	
	1250					1255						1260			
Glu	Asp	Ile	Val	Ala	Lys	Glu	Thr	Glu	Thr	Asp	Ile	Asp	Arg	Glu	
	1265					1270						1275			
Tyr	Phe	Thr	Thr	Ser	Ser	Pro	Pro	Ala	Thr	Gln	Pro	Thr	Arg	Pro	
	1280					1285						1290			
Pro	Thr	Val	Glu	Asp	Lys	Glu	Ala	Phe	Gly	Pro	Gln	Ala	Leu	Ser	
	1295					1300						1305			
Thr	Pro	Gln	Pro	Pro	Ala	Ser	Thr	Lys	Phe	His	Pro	Asp	Ile	Asn	
	1310					1315						1320			
Val	Tyr	Ile	Ile	Glu	Val	Arg	Glu	Asn	Lys	Thr	Gly	Arg	Met	Ser	
	1325					1330						1335			

Asp	Leu	Ser	Val	Ile	Gly	His	Pro	Ile	Asp	Ser	Glu	Ser	Lys	Glu
1340						1345					1350			
Asp	Glu	Pro	Cys	Ser	Glu	Glu	Thr	Asp	Pro	Val	His	Asp	Leu	Met
1355						1360					1365			
Ala	Glu	Ile	Leu	Pro	Glu	Phe	Pro	Asp	Ile	Ile	Glu	Ile	Asp	Leu
1370						1375					1380			
Tyr	His	Ser	Glu	Glu	Asn	Glu	Glu	Glu	Glu	Glu	Glu	Cys	Ala	Asn
1385						1390					1395			
Ala	Thr	Asp	Val	Thr	Thr	Thr	Pro	Ser	Val	Gln	Tyr	Ile	Asn	Gly
1400						1405					1410			
Lys	His	Leu	Val	Thr	Thr	Val	Pro	Lys	Asp	Pro	Glu	Ala	Ala	Glu
1415						1420					1425			
Ala	Arg	Arg	Gly	Gln	Phe	Glu	Ser	Val	Ala	Pro	Ser	Gln	Asn	Phe
1430						1435					1440			
Ser	Asp	Ser	Ser	Glu	Ser	Asp	Thr	His	Pro	Phe	Val	Ile	Ala	Lys
1445						1450					1455			
Thr	Glu	Leu	Ser	Thr	Ala	Val	Gln	Pro	Asn	Glu	Ser	Thr	Glu	Thr
1460						1465					1470			
Thr	Glu	Ser	Leu	Glu	Val	Thr	Trp	Lys	Pro	Glu	Thr	Tyr	Pro	Glu
1475						1480					1485			
Thr	Ser	Glu	His	Phe	Ser	Gly	Gly	Glu	Pro	Asp	Val	Phe	Pro	Thr
1490						1495					1500			
Val	Pro	Phe	His	Glu	Glu	Phe	Glu	Ser	Gly	Thr	Ala	Lys	Lys	Gly
1505						1510					1515			
Ala	Glu	Ser	Val	Thr	Glu	Arg	Asp	Thr	Glu	Val	Gly	His	Gln	Ala
1520						1525					1530			
His	Glu	His	Thr	Glu	Pro	Val	Ser	Leu	Phe	Pro	Glu	Glu	Ser	Ser
1535						1540					1545			
Gly	Glu	Ile	Ala	Ile	Asp	Gln	Glu	Ser	Gln	Lys	Ile	Ala	Phe	Ala
1550						1555					1560			
Arg	Ala	Thr	Glu	Val	Thr	Phe	Gly	Glu	Glu	Val	Glu	Lys	Ser	Thr
1565						1570					1575			
Ser	Val	Thr	Tyr	Thr	Pro	Thr	Ile	Val	Pro	Ser	Ser	Ala	Ser	Ala
1580						1585					1590			
Tyr	Val	Ser	Glu	Glu	Glu	Ala	Val	Thr	Leu	Ile	Gly	Asn	Pro	Trp
1595						1600					1605			
Pro	Asp	Asp	Leu	Leu	Ser	Thr	Lys	Glu	Ser	Trp	Val	Glu	Ala	Thr
1610						1615					1620			
Pro	Arg	Gln	Val	Val	Glu	Leu	Ser	Gly	Ser	Ser	Ser	Ile	Pro	Ile
1625						1630					1635			
Thr	Glu	Gly	Ser	Gly	Glu	Ala	Glu	Glu	Asp	Glu	Asp	Thr	Met	Phe
1640						1645					1650			
Thr	Met	Val	Thr	Asp	Leu	Ser	Gln	Arg	Asn	Thr	Thr	Asp	Thr	Leu
1655						1660					1665			
Ile	Thr	Leu	Asp	Thr	Ser	Arg	Ile	Ile	Thr	Glu	Ser	Phe	Phe	Glu
1670						1675					1680			
Val	Pro	Ala	Thr	Thr	Ile	Tyr	Pro	Val	Ser	Glu	Gln	Pro	Ser	Ala
1685						1690					1695			
Lys	Val	Val	Pro	Thr	Lys	Phe	Val	Ser	Glu	Thr	Asp	Thr	Ser	Glu
1700						1705					1710			
Trp	Ile	Ser	Ser	Thr	Thr	Val	Glu	Glu	Lys	Lys	Arg	Lys	Glu	Glu
1715						1720					1725			
Glu	Gly	Thr	Thr	Gly	Thr	Ala	Ser	Thr	Phe	Glu	Val	Tyr	Ser	Ser
1730						1735					1740			
Thr	Gln	Arg	Ser	Asp	Gln	Leu	Ile	Leu	Pro	Phe	Glu	Leu	Glu	Ser
1745						1750					1755			
Pro	Asn	Val	Ala	Thr	Ser	Ser	Asp	Ser	Gly	Thr	Arg	Lys	Ser	Phe
1760						1765					1770			
Met	Ser	Leu	Thr	Thr	Pro	Thr	Gln	Ser	Glu	Arg	Glu	Met	Thr	Asp
1775						1780					1785			
Ser	Thr	Pro	Val	Phe	Thr	Glu	Thr	Asn	Thr	Leu	Glu	Asn	Leu	Gly
1790						1795					1800			



Ala	Gln	Thr	Thr	Glu	His	Ser	Ser	Ile	His	Gln	Pro	Gly	Val	Gln
1805						1810					1815			
Glu	Gly	Leu	Thr	Thr	Leu	Pro	Arg	Ser	Pro	Ala	Ser	Val	Phe	Met
1820						1825					1830			
Glu	Gln	Gly	Ser	Gly	Glu	Ala	Ala	Ala	Asp	Pro	Glu	Thr	Thr	Thr
1835						1840					1845			
Val	Ser	Ser	Phe	Ser	Leu	Asn	Val	Glu	Tyr	Ala	Ile	Gln	Ala	Glu
1850						1855					1860			
Lys	Glu	Val	Ala	Gly	Thr	Leu	Ser	Pro	His	Val	Glu	Thr	Thr	Phe
1865						1870					1875			
Ser	Thr	Glu	Pro	Thr	Gly	Leu	Val	Leu	Ser	Thr	Val	Met	Asp	Arg
1880						1885					1890			
Val	Val	Ala	Glu	Asn	Ile	Thr	Gln	Thr	Ser	Arg	Glu	Ile	Val	Ile
1895						1900					1905			
Ser	Glu	Arg	Leu	Gly	Glu	Pro	Asn	Tyr	Gly	Ala	Glu	Ile	Arg	Gly
1910						1915					1920			
Phe	Ser	Thr	Gly	Phe	Pro	Leu	Glu	Glu	Asp	Phe	Ser	Gly	Asp	Phe
1925						1930					1935			
Arg	Glu	Tyr	Ser	Thr	Val	Ser	His	Pro	Ile	Ala	Lys	Glu	Glu	Thr
1940						1945					1950			
Val	Met	Met	Glu	Gly	Ser	Gly	Asp	Ala	Ala	Phe	Arg	Asp	Thr	Gln
1955						1960					1965			
Thr	Ser	Pro	Ser	Thr	Val	Pro	Thr	Ser	Val	His	Ile	Ser	His	Ile
1970						1975					1980			
Ser	Asp	Ser	Glu	Gly	Pro	Ser	Ser	Thr	Met	Val	Ser	Thr	Ser	Ala
1985						1990					1995			
Phe	Pro	Trp	Glu	Glu	Phe	Thr	Ser	Ser	Ala	Glu	Gly	Ser	Gly	Glu
2000						2005					2010			
Gln	Leu	Val	Thr	Val	Ser	Ser	Ser	Val	Val	Pro	Val	Leu	Pro	Ser
2015						2020					2025			
Ala	Val	Gln	Lys	Phe	Ser	Gly	Thr	Ala	Ser	Ser	Ile	Ile	Asp	Glu
2030						2035					2040			
Gly	Leu	Gly	Glu	Val	Gly	Thr	Val	Asn	Glu	Ile	Asp	Arg	Arg	Ser
2045						2050					2055			
Thr	Ile	Leu	Pro	Thr	Ala	Glu	Val	Glu	Gly	Thr	Lys	Ala	Pro	Val
2060						2065					2070			
Glu	Lys	Glu	Glu	Val	Lys	Val	Ser	Gly	Thr	Val	Ser	Thr	Asn	Phe
2075						2080					2085			
Pro	Gln	Thr	Ile	Glu	Pro	Ala	Lys	Leu	Trp	Ser	Arg	Gln	Glu	Val
2090						2095					2100			
Asn	Pro	Val	Arg	Gln	Glu	Ile	Glu	Ser	Glu	Thr	Thr	Ser	Glu	Glu
2105						2110					2115			
Gln	Ile	Gln	Glu	Glu	Lys	Ser	Phe	Glu	Ser	Pro	Gln	Asn	Ser	Pro
2120						2125					2130			
Ala	Thr	Glu	Gln	Thr	Ile	Phe	Asp	Ser	Gln	Thr	Phe	Thr	Glu	Thr
2135						2140					2145			
Glu	Leu	Lys	Thr	Thr	Asp	Tyr	Ser	Val	Leu	Thr	Thr	Lys	Lys	Thr
2150						2155					2160			
Tyr	Ser	Asp	Asp	Lys	Glu	Met	Lys	Glu	Glu	Asp	Thr	Ser	Leu	Val
2165						2170					2175			
Asn	Met	Ser	Thr	Pro	Asp	Pro	Asp	Ala	Asn	Gly	Leu	Glu	Ser	Tyr
2180						2185					2190			
Thr	Thr	Leu	Pro	Glu	Ala	Thr	Glu	Lys	Ser	His	Phe	Phe	Leu	Ala
2195						2200					2205			
Thr	Ala	Leu	Val	Thr	Glu	Ser	Ile	Pro	Ala	Glu	His	Val	Val	Thr
2210						2215					2220			
Asp	Ser	Pro	Ile	Lys	Lys	Glu	Glu	Ser	Thr	Lys	His	Phe	Pro	Lys
2225						2230					2235			
Gly	Met	Arg	Pro	Thr	Ile	Gln	Glu	Ser	Asp	Thr	Glu	Leu	Leu	Phe
2240						2245					2250			
Ser	Gly	Leu	Gly	Ser	Gly	Glu	Glu	Val	Leu	Pro	Thr	Leu	Pro	Thr
2255						2260					2265			

Glu	Ser	Val	Asn	Phe	Thr	Glu	Val	Glu	Gln	Ile	Asn	Asn	Thr	Leu
2270						2275					2280			
Tyr	Pro	His	Thr	Ser	Gln	Val	Glu	Ser	Thr	Ser	Ser	Asp	Lys	Ile
2285						2290					2295			
Glu	Asp	Phe	Asn	Arg	Met	Glu	Asn	Val	Ala	Lys	Glu	Val	Gly	Pro
2300						2305					2310			
Leu	Val	Ser	Gln	Thr	Asp	Ile	Phe	Glu	Gly	Ser	Gly	Ser	Val	Thr
2315						2320					2325			
Ser	Thr	Thr	Leu	Ile	Glu	Ile	Leu	Ser	Asp	Thr	Gly	Ala	Glu	Gly
2330						2335					2340			
Pro	Thr	Val	Ala	Pro	Leu	Pro	Phe	Ser	Thr	Asp	Ile	Gly	His	Pro
2345						2350					2355			
Gln	Asn	Gln	Thr	Val	Arg	Trp	Ala	Glu	Glu	Ile	Gln	Thr	Ser	Arg
2360						2365					2370			
Pro	Gln	Thr	Ile	Thr	Glu	Gln	Asp	Ser	Asn	Lys	Asn	Ser	Ser	Thr
2375						2380					2385			
Ala	Glu	Ile	Asn	Glu	Thr	Thr	Thr	Ser	Ser	Thr	Asp	Phe	Leu	Ala
2390						2395					2400			
Arg	Ala	Tyr	Gly	Phe	Glu	Met	Ala	Lys	Glu	Phe	Val	Thr	Ser	Ala
2405						2410					2415			
Pro	Lys	Pro	Ser	Asp	Leu	Tyr	Tyr	Glu	Pro	Ser	Gly	Glu	Gly	Ser
2420						2425					2430			
Gly	Glu	Val	Asp	Ile	Val	Asp	Ser	Phe	His	Thr	Ser	Ala	Thr	Thr
2435						2440					2445			
Gln	Ala	Thr	Arg	Gln	Glu	Ser	Ser	Thr	Thr	Phe	Val	Ser	Asp	Gly
2450						2455					2460			
Ser	Leu	Glu	Lys	His	Pro	Glu	Val	Pro	Ser	Ala	Lys	Ala	Val	Thr
2465						2470					2475			
Ala	Asp	Gly	Phe	Pro	Thr	Val	Ser	Val	Met	Leu	Pro	Leu	His	Ser
2480						2485					2490			
Glu	Gln	Asn	Lys	Ser	Ser	Pro	Asp	Pro	Thr	Ser	Thr	Leu	Ser	Asn
2495						2500					2505			
Thr	Val	Ser	Tyr	Glu	Arg	Ser	Thr	Asp	Gly	Ser	Phe	Gln	Asp	Arg
2510						2515					2520			
Phe	Arg	Glu	Phe	Glu	Asp	Ser	Thr	Leu	Lys	Pro	Asn	Arg	Lys	Lys
2525						2530					2535			
Pro	Thr	Glu	Asn	Ile	Ile	Ile	Asp	Leu	Asp	Lys	Glu	Asp	Lys	Asp
2540						2545					2550			
Leu	Ile	Leu	Thr	Ile	Thr	Glu	Ser	Thr	Ile	Leu	Glu	Ile	Leu	Pro
2555						2560					2565			
Glu	Leu	Thr	Ser	Asp	Lys	Asn	Thr	Ile	Ile	Asp	Ile	Asp	His	Thr
2570						2575					2580			
Lys	Pro	Val	Tyr	Glu	Asp	Ile	Leu	Gly	Met	Gln	Thr	Asp	Ile	Asp
2585						2590					2595			
Thr	Glu	Val	Pro	Ser	Glu	Pro	His	Asp	Ser	Asn	Asp	Glu	Ser	Asn
2600						2605					2610			
Asp	Asp	Ser	Thr	Gln	Val	Gln	Glu	Ile	Tyr	Glu	Ala	Ala	Val	Asn
2615						2620					2625			
Leu	Ser	Leu	Thr	Glu	Glu	Thr	Phe	Glu	Gly	Ser	Ala	Asp	Val	Leu
2630						2635					2640			
Ala	Ser	Tyr	Thr	Gln	Ala	Thr	His	Asp	Glu	Ser	Met	Thr	Tyr	Glu
2645						2650					2655			
Asp	Arg	Ser	Gln	Leu	Asp	His	Met	Gly	Phe	His	Phe	Thr	Thr	Gly
2660						2665					2670			
Ile	Pro	Ala	Pro	Ser	Thr	Glu	Thr	Glu	Leu	Asp	Val	Leu	Leu	Pro
2675						2680					2685			
Thr	Ala	Thr	Ser	Leu	Pro	Ile	Pro	Arg	Lys	Ser	Ala	Thr	Val	Ile
2690						2695					2700			
Pro	Glu	Ile	Glu	Gly	Ile	Lys	Ala	Glu	Ala	Lys	Ala	Leu	Asp	Asp
2705						2710					2715			
Met	Phe	Glu	Ser	Ser	Thr	Leu	Ser	Asp	Gly	Gln	Ala	Ile	Ala	Asp
2720						2725					2730			

Gln Ser	Glu Ile Ile Pro Thr	Leu Gly Gln Phe Glu	Arg Thr Gln
2735	2740	2745	
Glu Glu	Tyr Glu Asp Lys Lys	His Ala Gly Pro Ser	Phe Gln Pro
2750	2755	2760	
Glu Phe	Ser Ser Gly Ala Glu	Glu Ala Leu Val Asp	His Thr Pro
2765	2770	2775	
Tyr Leu	Ser Ile Ala Thr Thr	His Leu Met Asp Gln	Ser Val Thr
2780	2785	2790	
Glu Val	Pro Asp Val Met Glu	Gly Ser Asn Pro Pro	Tyr Tyr Thr
2795	2800	2805	
Asp Thr	Thr Leu Ala Val Ser	Thr Phe Ala Lys Leu	Ser Ser Gln
2810	2815	2820	
Thr Pro	Ser Ser Pro Leu Thr	Ile Tyr Ser Gly Ser	Glu Ala Ser
2825	2830	2835	
Gly His	Thr Glu Ile Pro Gln	Pro Ser Ala Leu Pro	Gly Ile Asp
2840	2845	2850	
Val Gly	Ser Ser Val Met Ser	Pro Gln Asp Ser Phe	Lys Glu Ile
2855	2860	2865	
His Val	Asn Ile Glu Ala Thr	Phe Lys Pro Ser Ser	Glu Glu Tyr
2870	2875	2880	
Leu His	Ile Thr Glu Pro Pro	Ser Leu Ser Pro Asp	Thr Lys Leu
2885	2890	2895	
Glu Pro	Ser Glu Asp Asp Gly	Lys Pro Glu Leu Leu	Glu Glu Met
2900	2905	2910	
Glu Ala	Ser Pro Thr Glu Leu	Ile Ala Val Glu Gly	Thr Glu Ile
2915	2920	2925	
Leu Gln	Asp Phe Gln Asn Lys	Thr Asp Gly Gln Val	Ser Gly Glu
2930	2935	2940	
Ala Ile	Lys Met Phe Pro Thr	Ile Lys Thr Pro Glu	Ala Gly Thr
2945	2950	2955	
Val Ile	Thr Thr Ala Asp Glu	Ile Glu Leu Glu Gly	Ala Thr Gln
2960	2965	2970	
Trp Pro	His Ser Thr Ser Ala	Ser Ala Thr Tyr Gly	Val Glu Ala
2975	2980	2985	
Gly Val	Val Pro Trp Leu Ser	Pro Gln Thr Ser Glu	Arg Pro Thr
2990	2995	3000	
Leu Ser	Ser Ser Pro Glu Ile	Asn Pro Glu Thr Gln	Ala Ala Leu
3005	3010	3015	
Ile Arg	Gly Gln Asp Ser Thr	Ile Ala Ala Ser Glu	Gln Gln Val
3020	3025	3030	
Ala Ala	Arg Ile Leu Asp Ser	Asn Asp Gln Ala Thr	Val Asn Pro
3035	3040	3045	
Val Glu	Phe Asn Thr Glu Val	Ala Thr Pro Pro Phe	Ser Leu Leu
3050	3055	3060	
Glu Thr	Ser Asn Glu Thr Asp	Phe Leu Ile Gly Ile	Asn Glu Glu
3065	3070	3075	
Ser Val	Glu Gly Thr Ala Ile	Tyr Leu Pro Gly Pro	Asp Arg Cys
3080	3085	3090	
Lys Met	Asn Pro Cys Leu Asn	Gly Gly Thr Cys Tyr	Pro Thr Glu
3095	3100	3105	
Thr Ser	Tyr Val Cys Thr Cys	Val Pro Gly Tyr Ser	Gly Asp Gln
3110	3115	3120	
Cys Glu	Leu Asp Phe Asp Glu	Cys His Ser Asn Pro	Cys Arg Asn
3125	3130	3135	
Gly Ala	Thr Cys Val Asp Gly	Phe Asn Thr Phe Arg	Cys Leu Cys
3140	3145	3150	
Leu Pro	Ser Tyr Val Gly Ala	Leu Cys Glu Gln Asp	Thr Glu Thr
3155	3160	3165	
Cys Asp	Tyr Gly Trp His Lys	Phe Gln Gly Gln Cys	Tyr Lys Tyr
3170	3175	3180	
Phe Ala	His Arg Arg Thr Trp	Asp Ala Ala Glu Arg	Glu Cys Arg
3185	3190	3195	

Leu	Gln	Gly	Ala	His	Leu	Thr	Ser	Ile	Leu	Ser	His	Glu	Glu	Gln
3200						3205					3210			
Met	Phe	Val	Asn	Arg	Val	Gly	His	Asp	Tyr	Gln	Trp	Ile	Gly	Leu
3215						3220					3225			
Asn	Asp	Lys	Met	Phe	Glu	His	Asp	Phe	Arg	Trp	Thr	Asp	Gly	Ser
3230						3235					3240			
Thr	Leu	Gln	Tyr	Glu	Asn	Trp	Arg	Pro	Asn	Gln	Pro	Asp	Ser	Phe
3245						3250					3255			
Phe	Ser	Ala	Gly	Glu	Asp	Cys	Val	Val	Ile	Ile	Trp	His	Glu	Asn
3260						3265					3270			
Gly	Gln	Trp	Asn	Asp	Val	Pro	Cys	Asn	Tyr	His	Leu	Thr	Tyr	Thr
3275						3280					3285			
Cys	Lys	Lys	Gly	Thr	Val	Ala	Cys	Gly	Gln	Pro	Pro	Val	Val	Glu
3290						3295					3300			
Asn	Ala	Lys	Thr	Phe	Gly	Lys	Met	Lys	Pro	Arg	Tyr	Glu	Ile	Asn
3305						3310					3315			
Ser	Leu	Ile	Arg	Tyr	His	Cys	Lys	Asp	Gly	Phe	Ile	Gln	Arg	His
3320						3325					3330			
Leu	Pro	Thr	Ile	Arg	Cys	Leu	Gly	Asn	Gly	Arg	Trp	Ala	Ile	Pro
3335						3340					3345			
Lys	Ile	Thr	Cys	Met	Asn	Pro	Ser	Ala	Tyr	Gln	Arg	Thr	Tyr	Ser
3350						3355					3360			
Met	Lys	Tyr	Phe	Lys	Asn	Ser	Ser	Ser	Ala	Lys	Asp	Asn	Ser	Ile
3365						3370					3375			
Asn	Thr	Ser	Lys	His	Asp	His	Arg	Trp	Ser	Arg	Arg	Trp	Gln	Glu
3380						3385					3390			
Ser	Arg	Arg	Met	Phe	Ile	Asn	Ile	Lys	Ser	Ile	Leu	Trp	Met	Cys
3395						3400					3405			
Ser	Thr	Leu	Ile	Val	Thr	His	Ala	Leu	His	Lys	Val	Lys	Val	Gly
3410						3415					3420			
Lys	Ser	Pro	Pro	Val	Arg	Gly	Ser	Leu	Ser	Gly	Lys	Val	Ser	Leu
3425						3430					3435			
Pro	Cys	His	Phe	Ser	Thr	Met	Pro	Thr	Leu	Pro	Pro	Ser	Tyr	Asn
3440						3445					3450			
Thr	Ser	Glu	Phe	Leu	Arg	Ile	Lys	Trp	Ser	Lys	Ile	Glu	Val	Asp
3455						3460					3465			
Lys	Asn	Gly	Lys	Asp	Leu	Lys	Glu	Thr	Thr	Val	Leu	Val	Ala	Gln
3470						3475					3480			
Asn	Gly	Asn	Ile	Lys	Ile	Gly	Gln	Asp	Tyr	Lys	Gly	Arg	Val	Ser
3485						3490					3495			
Val	Pro	Thr	His	Pro	Glu	Ala	Val	Gly	Asp	Ala	Ser	Leu	Thr	Val
3500						3505					3510			
Val	Lys	Leu	Leu	Ala	Ser	Asp	Ala	Gly	Leu	Tyr	Arg	Cys	Asp	Val
3515						3520					3525			
Met	Tyr	Gly	Ile	Glu	Asp	Thr	Gln	Asp	Thr	Val	Ser	Leu	Thr	Val
3530						3535					3540			
Asp	Gly	Val	Val	Phe	His	Tyr	Arg	Ala	Ala	Thr	Ser	Arg	Tyr	Thr
3545						3550					3555			
Leu	Asn	Phe	Glu	Ala	Ala	Gln	Lys	Ala	Cys	Leu	Asp	Val	Gly	Ala
3560						3565					3570			
Val	Ile	Ala	Thr	Pro	Glu	Gln	Leu	Phe	Ala	Ala	Tyr	Glu	Asp	Gly
3575						3580					3585			
Phe	Glu	Gln	Cys	Asp	Ala	Gly	Trp	Leu	Ala	Asp	Gln	Thr	Val	Arg
3590						3595					3600			
Tyr	Pro	Ile	Arg	Ala	Pro	Arg	Val	Gly	Cys	Tyr	Gly	Asp	Lys	Met
3605						3610					3615			
Gly	Lys	Ala	Gly	Val	Arg	Thr	Tyr	Gly	Phe	Arg	Ser	Pro	Gln	Glu
3620						3625					3630			
Thr	Tyr	Asp	Val	Tyr	Cys	Tyr	Val	Asp	His	Leu	Asp	Gly	Asp	Val
3635						3640					3645			
Phe	His	Leu	Thr	Val	Pro	Ser	Lys	Phe	Thr	Phe	Glu	Glu	Ala	Ala
3650						3655					3660			

Lys	Glu	Cys	Glu	Asn	Gln	Asp	Ala	Arg	Leu	Ala	Thr	Val	Gly	Glu
	3665					3670					3675			
Leu	Gln	Ala	Ala	Trp	Arg	Asn	Gly	Phe	Asp	Gln	Cys	Asp	Tyr	Gly
	3680					3685					3690			
Trp	Leu	Ser	Asp	Ala	Ser	Val	Arg	His	Pro	Val	Thr	Val	Ala	Arg
	3695					3700					3705			
Ala	Gln	Cys	Gly	Gly	Gly	Leu	Leu	Gly	Val	Arg	Thr	Leu	Tyr	Arg
	3710					3715					3720			
Phe	Glu	Asn	Gln	Thr	Gly	Phe	Pro	Pro	Pro	Asp	Ser	Arg	Phe	Asp
	3725					3730					3735			
Ala	Tyr	Cys	Phe	Lys	Pro	Lys	Glu	Ala	Thr	Thr	Ile	Asp	Leu	Ser
	3740					3745					3750			
Ile	Leu	Ala	Glu	Thr	Ala	Ser	Pro	Ser	Leu	Ser	Lys	Glu	Pro	Gln
	3755					3760					3765			
Met	Val	Ser	Asp	Arg	Thr	Thr	Pro	Ile	Ile	Pro	Leu	Val	Asp	Glu
	3770					3775					3780			
Leu	Pro	Val	Ile	Pro	Thr	Glu	Phe	Pro	Pro	Val	Gly	Asn	Ile	Val
	3785					3790					3795			
Ser	Phe	Glu	Gln	Lys	Ala	Thr	Val	Gln	Pro	Gln	Ala	Ile	Thr	Asp
	3800					3805					3810			
Ser	Leu	Ala	Thr	Lys	Leu	Pro	Thr	Pro	Thr	Gly	Ser	Thr	Lys	Lys
	3815					3820					3825			
Pro	Trp	Asp	Met	Asp	Asp	Tyr	Ser	Pro	Ser	Ala	Ser	Gly	Pro	Leu
	3830					3835					3840			
Gly	Lys	Leu	Asp	Ile	Ser	Glu	Ile	Lys	Glu	Glu	Val	Leu	Gln	Ser
	3845					3850					3855			
Thr	Thr	Gly	Val	Ser	His	Tyr	Ala	Thr	Asp	Ser	Trp	Asp	Gly	Val
	3860					3865					3870			
Val	Glu	Asp	Lys	Gln	Thr	Gln	Glu	Ser	Val	Thr	Gln	Ile	Glu	Gln
	3875					3880					3885			
Ile	Glu	Val	Gly	Pro	Leu	Val	Thr	Ser	Met	Glu	Ile	Leu	Lys	His
	3890					3895					3900			
Ile	Pro	Ser	Lys	Glu	Phe	Pro	Val	Thr	Glu	Thr	Pro	Leu	Val	Thr
	3905					3910					3915			
Ala	Arg	Met	Ile	Leu	Glu	Ser	Lys	Thr	Glu	Lys	Lys	Met	Val	Ser
	3920					3925					3930			
Thr	Val	Ser	Glu	Leu	Val	Thr	Thr	Gly	His	Tyr	Gly	Phe	Thr	Leu
	3935					3940					3945			
Gly	Glu	Glu	Asp	Asp	Glu	Asp	Arg	Thr	Leu	Thr	Val	Gly	Ser	Asp
	3950					3955					3960			
Glu	Ser	Thr	Leu	Ile	Phe	Asp	Gln	Ile	Pro	Glu	Val	Ile	Thr	Val
	3965					3970					3975			
Ser	Lys	Thr	Ser	Glu	Asp	Thr	Ile	His	Thr	His	Leu	Glu	Asp	Leu
	3980					3985					3990			
Glu	Ser	Val	Ser	Ala	Ser	Thr	Thr	Val	Ser	Pro	Leu	Ile	Met	Pro
	3995					4000					4005			

Pro	Ile	His	Val	Thr	Glu	Ser	Ser	Val	Glu	Met	Thr	Lys	Ser	Phe
4130						4135					4140			
Asp	Phe	Pro	Thr	Leu	Ile	Thr	Lys	Leu	Ser	Ala	Glu	Pro	Thr	Glu
4145						4150					4155			
Val	Arg	Asp	Met	Glu	Glu	Asp	Phe	Thr	Ala	Thr	Pro	Gly	Thr	Thr
4160						4165					4170			
Lys	Tyr	Asp	Glu	Asn	Ile	Thr	Thr	Val	Leu	Leu	Ala	His	Gly	Thr
4175						4180					4185			
Leu	Ser	Val	Glu	Ala	Ala	Thr	Val	Ser	Lys	Trp	Ser	Trp	Asp	Glu
4190						4195					4200			
Asp	Asn	Thr	Thr	Ser	Lys	Pro	Leu	Glu	Ser	Thr	Glu	Pro	Ser	Ala
4205						4210					4215			
Ser	Ser	Lys	Leu	Pro	Pro	Ala	Leu	Leu	Thr	Thr	Val	Gly	Met	Asn
4220						4225					4230			
Gly	Lys	Asp	Lys	Asp	Ile	Pro	Ser	Phe	Thr	Glu	Asp	Gly	Ala	Asp
4235						4240					4245			
Glu	Phe	Thr	Leu	Ile	Pro	Asp	Ser	Thr	Gln	Lys	Gln	Leu	Glu	Glu
4250						4255					4260			
Val	Thr	Asp	Glu	Asp	Ile	Ala	Ala	His	Gly	Lys	Phe	Thr	Ile	Arg
4265						4270					4275			
Phe	Gln	Pro	Thr	Thr	Ser	Thr	Gly	Ile	Ala	Glu	Lys	Ser	Thr	Leu
4280						4285					4290			
Arg	Asp	Ser	Thr	Thr	Glu	Glu	Lys	Val	Pro	Pro	Ile	Thr	Ser	Thr
4295						4300					4305			
Glu	Gly	Gln	Val	Tyr	Ala	Thr	Met	Glu	Gly	Ser	Ala	Leu	Gly	Glu
4310						4315					4320			
Val	Glu	Asp	Val	Asp	Leu	Ser	Lys	Pro	Val	Ser	Thr	Val	Pro	Gln
4325						4330					4335			
Phe	Ala	His	Thr	Ser	Glu	Val	Glu	Gly	Leu	Ala	Phe	Val	Ser	Tyr
4340						4345					4350			
Ser	Ser	Thr	Gln	Glu	Pro	Thr	Thr	Tyr	Val	Asp	Ser	Ser	His	Thr
4355						4360					4365			
Ile	Pro	Leu	Ser	Val	Ile	Pro	Lys	Thr	Asp	Trp	Gly	Val	Leu	Val
4370						4375					4380			
Pro	Ser	Val	Pro	Ser	Glu	Asp	Glu	Val	Leu	Gly	Glu	Pro	Ser	Gln
4385						4390					4395			
Asp	Ile	Leu	Val	Ile	Asp	Gln	Thr	Arg	Leu	Glu	Ala	Thr	Ile	Ser
4400						4405					4410			
Pro	Glu	Thr	Met	Arg	Thr	Thr	Lys	Ile	Thr	Glu	Gly	Thr	Thr	Gln
4415						4420					4425			
Glu	Glu	Phe	Pro	Trp	Lys	Glu	Gln	Thr	Ala	Glu	Lys	Pro	Val	Pro
4430						4435					4440			
Ala	Leu	Ser	Ser	Thr	Ala	Trp	Thr	Pro	Lys	Glu	Ala	Val	Thr	Pro
4445						4450					4455			
Leu	Asp	Glu	Gln	Glu	Gly	Asp	Gly	Ser	Ala	Tyr	Thr	Val	Ser	Glu
4460						4465					4470			
Asp	Glu	Leu	Leu	Thr	Gly	Ser	Glu	Arg	Val	Pro	Val	Leu	Glu	Thr
4475						4480					4485			
Thr	Pro	Val	Gly	Lys	Ile	Asp	His	Ser	Val	Ser	Tyr	Pro	Pro	Gly
4490						4495					4500			
Ala	Val	Thr	Glu	His	Lys	Val	Lys	Thr	Asp	Glu	Val	Val	Thr	Leu
4505						4510					4515			
Thr	Pro	Arg	Ile	Gly	Pro	Lys	Val	Ser	Leu	Ser	Pro	Gly	Pro	Glu
4520						4525					4530			
Gln	Lys	Tyr	Glu	Thr	Glu	Gly	Ser	Ser	Thr	Thr	Gly	Phe	Thr	Ser
4535						4540					4545			
Ser	Leu	Ser	Pro	Phe	Ser	Thr	His	Ile	Thr	Gln	Leu	Met	Glu	Glu
4550						4555					4560			
Thr	Thr	Thr	Glu	Lys	Thr	Ser	Leu	Glu	Asp	Ile	Asp	Leu	Gly	Ser
4565						4570					4575			
Gly	Leu	Phe	Glu	Lys	Pro	Lys	Ala	Thr	Glu	Leu	Ile	Glu	Phe	Ser
4580						4585					4590			

Thr	Ile	Lys	Val	Thr	Val	Pro	Ser	Asp	Ile	Thr	Thr	Ala	Phe	Ser
4595						4600					4605			
Ser	Val	Asp	Arg	Leu	His	Thr	Thr	Ser	Ala	Phe	Lys	Pro	Ser	Ser
4610						4615					4620			
Ala	Ile	Thr	Lys	Lys	Pro	Pro	Leu	Ile	Asp	Arg	Glu	Pro	Gly	Glu
4625						4630					4635			
Glu	Thr	Thr	Ser	Asp	Met	Val	Ile	Ile	Gly	Glu	Ser	Thr	Ser	His
4640						4645					4650			
Val	Pro	Pro	Thr	Thr	Leu	Glu	Asp	Ile	Val	Ala	Lys	Glu	Thr	Glu
4655						4660					4665			
Thr	Asp	Ile	Asp	Arg	Glu	Tyr	Phe	Thr	Thr	Ser	Ser	Pro	Pro	Ala
4670						4675					4680			
Thr	Gln	Pro	Thr	Arg	Pro	Pro	Thr	Val	Glu	Asp	Lys	Glu	Ala	Phe
4685						4690					4695			
Gly	Pro	Gln	Ala	Leu	Ser	Thr	Pro	Gln	Pro	Pro	Ala	Ser	Thr	Lys
4700						4705					4710			
Phe	His	Pro	Asp	Ile	Asn	Val	Tyr	Ile	Ile	Glu	Val	Arg	Glu	Asn
4715						4720					4725			
Lys	Thr	Gly	Arg	Met	Ser	Asp	Leu	Ser	Val	Ile	Gly	His	Pro	Ile
4730						4735					4740			
Asp	Ser	Glu	Ser	Lys	Glu	Asp	Glu	Pro	Cys	Ser	Glu	Glu	Thr	Asp
4745						4750					4755			
Pro	Val	His	Asp	Leu	Met	Ala	Glu	Ile	Leu	Pro	Glu	Phe	Pro	Asp
4760						4765					4770			
Ile	Ile	Glu	Ile	Asp	Leu	Tyr	His	Ser	Glu	Glu	Asn	Glu	Glu	Glu
4775						4780					4785			
Glu	Glu	Glu	Cys	Ala	Asn	Ala	Thr	Asp	Val	Thr	Thr	Thr	Pro	Ser
4790						4795					4800			
Val	Gln	Tyr	Ile	Asn	Gly	Lys	His	Leu	Val	Thr	Thr	Val	Pro	Lys
4805						4810					4815			
Asp	Pro	Glu	Ala	Ala	Glu	Ala	Arg	Arg	Gly	Gln	Phe	Glu	Ser	Val
4820						4825					4830			
Ala	Pro	Ser	Gln	Asn	Phe	Ser	Asp	Ser	Ser	Glu	Ser	Asp	Thr	His
4835						4840					4845			
Pro	Phe	Val	Ile	Ala	Lys	Thr	Glu	Leu	Ser	Thr	Ala	Val	Gln	Pro
4850						4855					4860			
Asn	Glu	Ser	Thr	Glu	Thr	Thr	Glu	Ser	Leu	Glu	Val	Thr	Trp	Lys
4865						4870					4875			
Pro	Glu	Thr	Tyr	Pro	Glu	Thr	Ser	Glu	His	Phe	Ser	Gly	Gly	Glu
4880						4885					4890			
Pro	Asp	Val	Phe	Pro	Thr	Val	Pro	Phe	His	Glu	Glu	Phe	Glu	Ser
4895						4900					4905			
Gly	Thr	Ala	Lys	Lys	Gly	Ala	Glu	Ser	Val	Thr	Glu	Arg	Asp	Thr
4910						4915					4920			
Glu	Val	Gly	His	Gln	Ala	His	Glu	His	Thr	Glu	Pro	Val	Ser	Leu
4925						4930					4935			

Asn	Thr	Thr	Asp	Thr	Leu	Ile	Thr	Leu	Asp	Thr	Ser	Arg	Ile	Ile
5060						5065					5070			
Thr	Glu	Ser	Phe	Phe	Glu	Val	Pro	Ala	Thr	Thr	Ile	Tyr	Pro	Val
5075						5080					5085			
Ser	Glu	Gln	Pro	Ser	Ala	Lys	Val	Val	Pro	Thr	Lys	Phe	Val	Ser
5090						5095					5100			
Glu	Thr	Asp	Thr	Ser	Glu	Trp	Ile	Ser	Ser	Thr	Thr	Val	Glu	Glu
5105						5110					5115			
Lys	Lys	Arg	Lys	Glu	Glu	Glu	Gly	Thr	Thr	Gly	Thr	Ala	Ser	Thr
5120						5125					5130			
Phe	Glu	Val	Tyr	Ser	Ser	Thr	Gln	Arg	Ser	Asp	Gln	Leu	Ile	Leu
5135						5140					5145			
Pro	Phe	Glu	Leu	Glu	Ser	Pro	Asn	Val	Ala	Thr	Ser	Ser	Asp	Ser
5150						5155					5160			
Gly	Thr	Arg	Lys	Ser	Phe	Met	Ser	Leu	Thr	Thr	Pro	Thr	Gln	Ser
5165						5170					5175			
Glu	Arg	Glu	Met	Thr	Asp	Ser	Thr	Pro	Val	Phe	Thr	Glu	Thr	Asn
5180						5185					5190			
Thr	Leu	Glu	Asn	Leu	Gly	Ala	Gln	Thr	Thr	Glu	His	Ser	Ser	Ile
5195						5200					5205			
His	Gln	Pro	Gly	Val	Gln	Glu	Gly	Leu	Thr	Thr	Leu	Pro	Arg	Ser
5210						5215					5220			
Pro	Ala	Ser	Val	Phe	Met	Glu	Gln	Gly	Ser	Gly	Glu	Ala	Ala	Ala
5225						5230					5235			
Asp	Pro	Glu	Thr	Thr	Thr	Val	Ser	Ser	Phe	Ser	Leu	Asn	Val	Glu
5240						5245					5250			
Tyr	Ala	Ile	Gln	Ala	Glu	Lys	Glu	Val	Ala	Gly	Thr	Leu	Ser	Pro
5255						5260					5265			
His	Val	Glu	Thr	Thr	Phe	Ser	Thr	Glu	Pro	Thr	Gly	Leu	Val	Leu
5270						5275					5280			
Ser	Thr	Val	Met	Asp	Arg	Val	Val	Ala	Glu	Asn	Ile	Thr	Gln	Thr
5285						5290					5295			
Ser	Arg	Glu	Ile	Val	Ile	Ser	Glu	Arg	Leu	Gly	Glu	Pro	Asn	Tyr
5300						5305					5310			
Gly	Ala	Glu	Ile	Arg	Gly	Phe	Ser	Thr	Gly	Phe	Pro	Leu	Glu	Glu
5315						5320					5325			
Asp	Phe	Ser	Gly	Asp	Phe	Arg	Glu	Tyr	Ser	Thr	Val	Ser	His	Pro
5330						5335					5340			
Ile	Ala	Lys	Glu	Glu	Thr	Val	Met	Met	Glu	Gly	Ser	Gly	Asp	Ala
5345						5350					5355			
Ala	Phe	Arg	Asp	Thr	Gln	Thr	Ser	Pro	Ser	Thr	Val	Pro	Thr	Ser
5360						5365					5370			
Val	His	Ile	Ser	His	Ile	Ser	Asp	Ser	Glu	Gly	Pro	Ser	Ser	Thr
5375						5380					5385			
Met	Val	Ser	Thr	Ser	Ala	Phe	Pro	Trp	Glu	Glu	Phe	Thr	Ser	Ser
5390						5395					5400			
Ala	Glu	Gly	Ser	Gly	Glu	Gln	Leu	Val	Thr	Val	Ser	Ser	Ser	Val
5405						5410					5415			
Val	Pro	Val	Leu	Pro	Ser	Ala	Val	Gln	Lys	Phe	Ser	Gly	Thr	Ala
5420						5425					5430			
Ser	Ser	Ile	Ile	Asp	Glu	Gly	Leu	Gly	Glu	Val	Gly	Thr	Val	Asn
5435						5440					5445			
Glu	Ile	Asp	Arg	Arg	Ser	Thr	Ile	Leu	Pro	Thr	Ala	Glu	Val	Glu
5450						5455					5460			
Gly	Thr	Lys	Ala	Pro	Val	Glu	Lys	Glu	Glu	Val	Lys	Val	Ser	Gly
5465						5470					5475			
Thr	Val	Ser	Thr	Asn	Phe	Pro	Gln	Thr	Ile	Glu	Pro	Ala	Lys	Leu
5480						5485					5490			
Trp	Ser	Arg	Gln	Glu	Val	Asn	Pro	Val	Arg	Gln	Glu	Ile	Glu	Ser
5495						5500					5505			
Glu	Thr	Thr	Ser	Glu	Glu	Ile	Ile	Gln	Glu	Glu	Lys	Ser	Phe	Glu
5510						5515					5520			



Ser	Pro	Gln	Asn	Ser	Pro	Ala	Thr	Glu	Gln	Thr	Ile	Phe	Asp	Ser
5525						5530					5535			
Gln	Thr	Phe	Thr	Glu	Thr	Glu	Leu	Lys	Thr	Thr	Asp	Tyr	Ser	Val
5540						5545					5550			
Leu	Thr	Thr	Lys	Lys	Thr	Tyr	Ser	Asp	Asp	Lys	Glu	Met	Lys	Glu
5555						5560					5565			
Glu	Asp	Thr	Ser	Leu	Val	Asn	Met	Ser	Thr	Pro	Asp	Pro	Asp	Ala
5570						5575					5580			
Asn	Gly	Leu	Glu	Ser	Tyr	Thr	Thr	Leu	Pro	Glu	Ala	Thr	Glu	Lys
5585						5590					5595			
Ser	His	Phe	Phe	Leu	Ala	Thr	Ala	Leu	Val	Thr	Glu	Ser	Ile	Pro
5600						5605					5610			
Ala	Glu	His	Val	Val	Thr	Asp	Ser	Pro	Ile	Lys	Lys	Glu	Glu	Ser
5615						5620					5625			
Thr	Lys	His	Phe	Pro	Lys	Gly	Met	Arg	Pro	Thr	Ile	Gln	Glu	Ser
5630						5635					5640			
Asp	Thr	Glu	Leu	Leu	Phe	Ser	Gly	Leu	Gly	Ser	Gly	Glu	Glu	Val
5645						5650					5655			
Leu	Pro	Thr	Leu	Pro	Thr	Glu	Ser	Val	Asn	Phe	Thr	Glu	Val	Glu
5660						5665					5670			
Gln	Ile	Asn	Asn	Thr	Leu	Tyr	Pro	His	Thr	Ser	Gln	Val	Glu	Ser
5675						5680					5685			
Thr	Ser	Ser	Asp	Lys	Ile	Glu	Asp	Phe	Asn	Arg	Met	Glu	Asn	Val
5690						5695					5700			
Ala	Lys	Glu	Val	Gly	Pro	Leu	Val	Ser	Gln	Thr	Asp	Ile	Phe	Glu
5705						5710					5715			
Gly	Ser	Gly	Ser	Val	Thr	Ser	Thr	Thr	Leu	Ile	Glu	Ile	Leu	Ser
5720						5725					5730			
Asp	Thr	Gly	Ala	Glu	Gly	Pro	Thr	Val	Ala	Pro	Leu	Pro	Phe	Ser
5735						5740					5745			
Thr	Asp	Ile	Gly	His	Pro	Gln	Asn	Gln	Thr	Val	Arg	Trp	Ala	Glu
5750						5755					5760			
Glu	Ile	Gln	Thr	Ser	Arg	Pro	Gln	Thr	Ile	Thr	Glu	Gln	Asp	Ser
5765						5770					5775			
Asn	Lys	Asn	Ser	Ser	Thr	Ala	Glu	Ile	Asn	Glu	Thr	Thr	Thr	Ser
5780						5785					5790			
Ser	Thr	Asp	Phe	Leu	Ala	Arg	Ala	Tyr	Gly	Phe	Glu	Met	Ala	Lys
5795						5800					5805			
Glu	Phe	Val	Thr	Ser	Ala	Pro	Lys	Pro	Ser	Asp	Leu	Tyr	Tyr	Glu
5810						5815					5820			
Pro	Ser	Gly	Glu	Gly	Ser	Gly	Glu	Val	Asp	Ile	Val	Asp	Ser	Phe
5825						5830					5835			
His	Thr	Ser	Ala	Thr	Thr	Gln	Ala	Thr	Arg	Gln	Glu	Ser	Ser	Thr
5840						5845					5850			
Thr	Phe	Val	Ser	Asp	Gly	Ser	Leu	Glu	Lys	His	Pro	Glu	Val	Pro
5855						5860					5865			
Ser	Ala	Lys	Ala	Val	Thr	Ala	Asp	Gly	Phe	Pro	Thr	Val	Ser	Val
5870						5875					5880			
Met	Leu	Pro	Leu	His	Ser	Glu	Gln	Asn	Lys	Ser	Ser	Pro	Asp	Pro
5885						5890					5895			
Thr	Ser	Thr	Leu	Ser	Asn	Thr	Val	Ser	Tyr	Glu	Arg	Ser	Thr	Asp
5900						5905					5910			
Gly	Ser	Phe	Gln	Asp	Arg	Phe	Arg	Glu	Phe	Glu	Asp	Ser	Thr	Leu
5915						5920					5925			
Lys	Pro	Asn	Arg	Lys	Lys	Pro	Thr	Glu	Asn	Ile	Ile	Ile	Asp	Leu
5930						5935					5940			
Asp	Lys	Glu	Asp	Lys	Asp	Leu	Ile	Leu	Thr	Ile	Thr	Glu	Ser	Thr
5945						5950					5955			
Ile	Leu	Glu	Ile	Leu	Pro	Glu	Leu	Thr	Ser	Asp	Lys	Asn	Thr	Ile
5960						5965					5970			
Ile	Asp	Ile	Asp	His	Thr	Lys	Pro	Val	Tyr	Glu	Asp	Ile	Leu	Gly
5975						5980					5985			

Met	Gln	Thr	Asp	Ile	Asp	Thr	Glu	Val	Pro	Ser	Glu	Pro	His	Asp
5990						5995					6000			
Ser	Asn	Asp	Glu	Ser	Asn	Asp	Asp	Ser	Thr	Gln	Val	Gln	Glu	Ile
6005						6010					6015			
Tyr	Glu	Ala	Ala	Val	Asn	Leu	Ser	Leu	Thr	Glu	Glu	Thr	Phe	Glu
6020						6025					6030			
Gly	Ser	Ala	Asp	Val	Leu	Ala	Ser	Tyr	Thr	Gln	Ala	Thr	His	Asp
6035						6040					6045			
Glu	Ser	Met	Thr	Tyr	Glu	Asp	Arg	Ser	Gln	Leu	Asp	His	Met	Gly
6050						6055					6060			
Phe	His	Phe	Thr	Thr	Gly	Ile	Pro	Ala	Pro	Ser	Thr	Glu	Thr	Glu
6065						6070					6075			
Leu	Asp	Val	Leu	Leu	Pro	Thr	Ala	Thr	Ser	Leu	Pro	Ile	Pro	Arg
6080						6085					6090			
Lys	Ser	Ala	Thr	Val	Ile	Pro	Glu	Ile	Glu	Gly	Ile	Lys	Ala	Glu
6095						6100					6105			
Ala	Lys	Ala	Leu	Asp	Asp	Met	Phe	Glu	Ser	Ser	Thr	Leu	Ser	Asp
6110						6115					6120			
Gly	Gln	Ala	Ile	Ala	Asp	Gln	Ser	Glu	Ile	Ile	Pro	Thr	Leu	Gly
6125						6130					6135			
Gln	Phe	Glu	Arg	Thr	Gln	Glu	Glu	Tyr	Glu	Asp	Lys	Lys	His	Ala
6140						6145					6150			
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